

# SCIENCE

FRIDAY, MAY 18, 1945

No. 2629

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## SHALL WE LOSE OR KEEP OUR PLANT AND ANIMAL STOCKS

By Professor WALTER LANDAUER

THE UNIVERSITY OF CONNECTICUT, STORRS, CONN.

GENETICISTS have learned to produce hereditary variations at will; they have succeeded in multiplying greatly the frequency with which mutations occur; but they have not yet brought under control the direction of these events. The future may well hold the secret of how to overcome the randomness of changes in the hereditary substratum of organisms, and we may thereby master the fashioning of plants and animals "according to plan." Until this time has arrived, however, we shall do well to keep in mind the words of William Bateson, "Variation leads; the breeder follows." The art of breeding, the art of producing new combinations of genes, rests entirely on the raw materials—the mutations—as they are provided by nature.

The uses to which new mutations and varied gene combinations may be put are manifold. Geneticists and biologists generally seek material which will aid in an analysis of development and evolution. Students of human and veterinary medicine are interested in those forms of life which are most likely to contribute to the understanding and control of disease. Breeders of livestock and of crop or ornamental plants search for types which will enhance the pleasures and profits to be derived from their stocks by heightened disease resistance, greater vigor, increased yields or particular esthetic values. The present war has dramatized the need of various industries for plant materials with specified qualities, many of which could not be obtained. Stocks which

give specific and constant responses to drugs and other chemicals should have great potential value for manufacturers of pharmaceutical preparations and for assay and control laboratories. In short, for whatever purposes plants or animals are used by man, one may always expect that the value of particular types can be enhanced by improvements in their hereditary constitution. Moreover, in all fundamental work concerning animal and plant genetics, whether such investigations are concerned with the nature of the gene, linkage relations or other problems, it is of utmost importance that mutant stocks should be perpetuated for research purposes. The mutations which geneticists isolate and describe thus become at once the tools of theoretical and of applied biology, and the wise craftsman treasures his tools.

It is necessary to emphasize once again that these are tools which we can isolate and use in reshuffling the design of organisms, but which we can not create to order. This is a situation very different from that obtaining in other fields. All industrial developments are rooted in our knowledge concerning the physical and chemical nature of substances and the laws which govern their relations and interactions. This knowledge enables man to invent tools and machines and to synthesize all manner of new chemical compounds. Designs and patterns, models and formulae precede production, and these plans make it possible at any time to recreate the products of human invention. Steady and uninterrupted progress of industrial development is assured by the knowledge of raw materials and the blueprints of inventors which are handed on from generation to generation.

In contrast, the geneticist can not build with the knowledge of his predecessors unless he possesses also the necessary building stones, the mutants. Yet, all too frequently such mutants are allowed to become extinct. This is a common occurrence with research stocks after they have served the purposes of a particular investigator; it happens frequently with varieties of all kinds of plants which, with much labor and expense, had been collected in far-off countries, and with strains which had been isolated by breeders but had not given prospect of immediate returns.

Sooner or later many such extinct stocks will acquire renewed interest on account of fresh evidence. They will then be sought in vain. It is clearly impossible for the individual investigator or breeder or for any single laboratory to perpetuate stocks which are no longer used in their research program. The duty to do so rests with the groups which are interested in particular forms of animals or plants and with society at large.

This is a situation of long standing. More than 25 years ago the National Research Council was first ap-

proached to intervene with a specific program of stock maintenance. Nothing was done at that time. Later on, the maize and *Drosophila*-geneticists initiated group activities of their own and established stock centers from which every research worker now can be supplied, on short notice, with any particular mutation which he may need for his work.

The widespread use of maize and *Drosophila* in genetic research is accounted for by many advantages peculiar to these organisms, such as large size of the ear and the possibility of self- or cross-fertilization in corn, shortness of the life cycle in the fruit-fly, the great number of available mutants and relatively simple cytology of both. In the majority of other plants and animals the situation is less favorable, and this calls for even closer group cooperation and for more liberal financial support.

Heredity variants of plants and animals belong to our most valuable natural resources. It is to be hoped that the protracted neglect of soil conservation will not be repeated in the biological domain. Only within recent years has it become acknowledged by all parties concerned that "to pass the soil on to succeeding generations as nearly unimpaired as possible is generally recognized as a worthy public purpose."<sup>1</sup> The basic consideration for soil conservation activities has been aptly formulated, as follows. "So far as agriculture is concerned, however, the case for saving all or most of the topsoil rests on the same principles as an accident or health insurance policy. Part of the soil may never be needed, but this is not certain. The premium required for protection against the uncertain hazards of the future should be paid, if it is not too large."<sup>1</sup> The purpose of such policies is to protect the interests of the immediate as well as those of the more remote future and "to be successful, an adequate soil-conservation program must serve the farmers' interest as well as the public interest."

These statements can be applied directly to the problems of preserving and maintaining stocks of plants and animals. We must look forward to the day when, to speak with Henry A. Wallace, "humanity will take as great an interest in the creation of superior forms of life as it has taken in past years in the perfection of superior forms of machinery," and if we are to be ready on that day to begin creative work on a large scale we must husband our resources now. It will be impossible, of course, to preserve each mutant and to maintain every strain and variety of all plants and animals. What deserves to be preserved must be decided by those who are in the best position to judge. But it is certainly in the interest of society that any stock should be propa-

<sup>1</sup> U.S.D.A. Yearbook of Agriculture, 1938.

ated which might have future value for science, agriculture or industry.

From a practical point of view the development of hybrid corn is probably the greatest contribution which genetics has made to agriculture. The production of hybrid seed involves the maintenance of many stocks which by themselves would be of relatively little value. They are preserved because it is profitable to do so. There is no doubt, however, that many stocks which in the past have been allowed to become extinct or which, in the absence of facilities for maintenance, will disappear in the future, might easily be of importance comparable to the maize stocks which are used in producing hybrid corn. It can not be emphasized too strongly that the future usefulness of many stocks and mutants can not be foreseen. The introduction of plant and animal species into regions which they have not been cultivated previously, the despread occurrence of infectious diseases with the consequent need of finding or creating resistant stocks, and other conditions may at any time focus the breeder's interest on types which, until then, had not been considered profitable. Post-war conditions will almost certainly create a demand for new kinds and varieties of plants and animals for agricultural and industrial use. Provisions which anticipate these and subsequent requirements should be made now.

Certain needs are with us already, however, which

call for the creative ingenuity of geneticists. The accuracy and reliability of much of the work of physiologists, pharmacologists and experimental pathologists depends largely on the uniformity of response of their experimental animals to particular conditions. Few investigators will seriously defend the proposition that alley cats are proper material for quantitative tests, that dogs from city pounds are ideal experimental animals or that one rabbit equals another irrespective of its genetic constitution. Yet, the majority of university, industrial and government laboratories everywhere proceed as if genetic uniformity were of no consequence in their experiments or assays. It is the duty of geneticists to underscore the dangers of such an attitude. It is their duty also, of course, to provide the proper stocks, but the initiation of such necessarily costly undertakings must presumably wait until sufficient interest has been aroused to provide for a sound financial basis.

Some years ago the National Research Council created a "Committee on the Maintenance of Pure Genetic Strains," recently renamed "Committee on Plant and Animal Stocks," of which the writer has the honor to be chairman. The problems which have been discussed in the preceding paragraphs are of great concern to this committee and any information which has a bearing on these problems will help the committee in its work.

## DISEASE OF THE HEART. II

By Dr. ALFRED E. COHN

MEMBER EMERITUS, THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK

What has now been passed in review concerns the several structural elements of the heart—its muscle, its vascular systems, its inner and outer coverings, its valves, its nerves and ganglia. It seems odd that the first recognizable description of a disease of the heart, made by Morgagni, should depend on the last of its structural elements to be discovered—heart block depending on the severance of the auriculoventricular conducting system. This first discovery came late. Dates are in fact not uninteresting. Morgagni (1682–1771) was born when Newton (1642–1727) was forty years old. Newton lived on till eighty-five. Morgagni's observation, clearly, was not based on knowledge of the existence of this system, which was not described until 1903. What he observed was slowness of the pulse and attacks of epilepsy.

But that was nevertheless the first statement about cardiac disease which is still identifiable. Next in the order of the time came suggestions about the meaning of rheumatic fever. Pitcairn began to talk

about the possibility of such a relation to disease of the cardiac valves in 1788. Wells, a native of South Carolina, a loyalist who returned to England, made record of this belief of Pitcairn's in 1812, though Baillie referred to Pitcairn's teaching even earlier, in 1797. That was a year after Jenner published his book on vaccination against smallpox. In all probability it was not until 1832, however, when James Hope specified "inflammation of the internal membrane of the heart, resulting from carditis, pericarditis—especially rheumatic—from fever or from any other cause" that the influence of rheumatic fever upon the valves of the heart was put forward in clear anatomical terms. Even if Pitcairn knew that rheumatic fever affected the heart, he had not the means of ascertaining that relation clinically. To do this required that genial device introduced by Laennec in 1819. With his stethoscope one could hear what was going on. It does not matter that Laennec did not identify correctly the valves which account respectively for the first and second sounds, nor had

the time for specifying the meaning of murmurs come yet. It remained for Hope to establish these facts—by experiment. Laennec's contemporary, Corvisart (1755–1821), physician to the first Napoleon, was the first to insist that hearts could be large and so contributed the suggestion that the size of the heart, which means in essence its muscular mass, is somehow the central theme of the puzzle of cardiac disease. His book was published in 1806. In ascertaining the facts about size Corvisart relied upon a discovery by Auenbrugger, to whom he gave full credit for his indebtedness. Percussion was described by Auenbrugger in 1761, six years after Corvisart was born.

Two other additions have been made to knowledge of disease of the heart. One is the discovery of the auriculo-ventricular bundle by William His, Jr., an anatomical discovery, interest in which dates from the days of Morgagni, and later from those of Stokes and Adams, until its nature and its manifestations have now finally become very clear. The second is James Herrick's observation that a diagnosis can be made, even during life, of the occlusion, partial and also complete, of a branch of a coronary artery. The fact that a complaint called vaguely angina pectoris plus the subsequent discovery of a lesion in his coronary artery coexisted in the case of John Hunter and indeed in many another patient does not in itself constitute, I think, a valid claim that a disease has been discovered or described. John Hunter, having been himself so insistent on the meaning of the relation to each other of structure and behavior, would no doubt have taken this same view.

All these pieces of information and the conceptions of disease which have been built upon them did not begin to take shape, it must be clear, until less than two hundred years ago. In very recent times the knowledge which has been gained in the past has been consolidated. There has been notable acceleration, and this acceleration holds forth promise—promise of still more important things to come.

I omit intentionally from consideration, as I have already said, many matters usually included in an account of disease—discoveries which belong properly to anatomy or physiology or chemistry. These are no doubt children of that "medicine" which is the mother of all the sciences. Many a mother, like this one, is full of pride in the beauty of her offspring. But she knows she has her own work to do and that her children have theirs. They, mother and children, give and take, but the worth of each one is his own. When I speak of medicine, I speak of diseases and the study of diseases. I do not speak of other sciences. I do this the more deliberately because there is involved here a conception of how the study of

diseases is to go forward. It is to go forward in the hospital where it is in its own home and not in the homes of children or grandchildren. It is enough that we visit mutually, perhaps even for long stretches, and are welcome, mutually. Every excursion though implies returning home. The moral here is, I believe, of transcendent importance.

Our historical overeagerness sometimes, as in the case of Morgagni and heart-block, precipitates us into recognitions and attributions and credit for full-dress discoveries, on evidence often a little tenuous. The words of Hope on rheumatic cardiac disease, in 1832, are still not definitive enough to convince us that he meant what we do when we speak of the association of rheumatic fever with disorganization of the cardiac valves. In recounting these matters what I am thinking is, that unless conceptions are firmly based on observation both of abnormal anatomical structure and of clinical misbehavior, such observations can not be used as the building blocks of an edifice of enduring significance to be known as a disease. Form and function must needs complement each other, be thought of in terms of each other, in order that a description of an ailment may entitle it to qualify in the family of diseases.

During these years there has been no idleness in the invention of tools used to make more precise the detection of those errors in behavior to which the heart is liable. Among these tools are important pieces of apparatus. There are pieces of apparatus to inscribe the pulse; pieces of apparatus to measure the pressure under which the blood stream flows; the x-rays with which to look through the chest and to photograph the shadows which the heart casts, and more recently casts upon a moving film whereon the extent of individual contractions at each point of its outline can be observed; pieces of apparatus which measure accurately changes in volume of small anatomical parts, like ears and tips of fingers and toes—a technical contribution which has issued from this, the Tulane School of Medicine. Among these pieces of apparatus are the inventions of the electrometer of Lippmann and of the string galvanometer of Einthoven, which through registering action currents detect irregularities in the beat of the heart, of both auricles and ventricles. These pieces of apparatus are mechanically reliable. The string galvanometer yields reproducible curves which, because the usual normal forms are now known, give information on deviations from normal. This result can occur because of the togetherness in action which all the diverse complicated parts of the heart achieve in forming a usual, normal single heart beat. When the usual form is absent, the inference is that some part of the muscle of the heart has defaulted either in

ole or in part. The result is alteration in the normal form of the electrical curve. If the continuity of the auriculo-ventricular system is disrupted, this is documented in the curve which suffers in still other way. The usual sequence in contraction of auricles and ventricles is disturbed or disappears. This is the condition known as heart-block, of which there are a number of forms.

We possess then a collection of instruments for examination which give information on the sufficiency of the valves and also in a limited way of the muscle fiber when the valves are subject to one or another kind of damage; when they are sclerotic or congenitally deformed or infected; and when the muscle, either because of strain resulting from defective valves or because of defects in nutrition which so often takes place when the patency of the arteries is compromised.

It is a matter of much concern that so far there is no method of investigation which measures the performance of the muscle, where after all the power of the machine resides. The absence of such an instrument is not, however, an oversight. It must be attributed to the intellectual competence of James Mackenzie that he studied the irregularities of the heart beat, simultaneously with Wenckebach, because he discovered in women in labor that their hearts, when they seemed to be failing often exhibited irregularity of beat. To Mackenzie it seemed a near thought that irregularity might be related to failure in contractile power. It is to the further credit of this great man that he was among the first, perhaps the first, to recognize that the existence of irregularity gave no necessary evidence on the presence of heart failure.

Einthoven also entertained this interest in contractile power. He approached its analysis from a different angle. In recording variations in electrical potential it was his idea and hope that, as an expression of contraction, this might exhibit variations that could be correlated with alteration in the muscular power of the heart. The galvanometer which he constructed, the form in general clinical use, failed however to yield that kind of information. He constructed therefore another form of apparatus calculated to respond mechanically to muscular motion even when expressive of the slightest contraction. In his endeavor he succeeded, but for practical purposes the failure persisted. This was owing not to failure in mechanical ingenuity but to refractoriness inherent in this situation. When electrical energy is measured that originates in so special a form of contractile power, as is possessed by the mammalian heart, the results can not run parallel with the contractile act. Undoubtedly the end of endeavors in this direction has not yet come.

So much attention has been devoted to describing the muscle and the blood vessels of the heart for a definite reason. The problem is whether older men are or can be normal. If not, the question would then be, are only healthy young men normal, and if so, are they so at one age only, or during a certain span of years? Older men die through failure of the heart, in many, perhaps in most cases, though of this there is no knowledge, because there is no possibility of detecting what has gone wrong specifically with its contractile mechanism. The reason for this inquiry issues from that same curve of mortality to which I have referred. That curve declares, cancer excepted, that malfunction of the heart or of the vascular system is the only remaining cause exhibiting significant numerical magnitude as an occasion for death. This form of dying, called intrinsic in nature, was set over against those forms regarded as being extraneous in origin.

This form of death in the aged in a strict sense is physiological death or, if you please, anatomical. If living is natural and normal, and if growing also is, this end to life may be said to be a natural result and therefore not an example of disease. Growth constitutes then continuous differentiation, and the problem of cardiac failure in the old becomes a problem of growth and is therefore not a problem of disease. The problem is a problem of understanding, in a biological sense, and involves inferentially a definition of disease.

The task of statesmen concerned with the public health is care for the welfare of human beings in suffering, and to protect the public, when possible, against the ravages of contagion. It begins to appear as if death from any other cause than from cardiovascular ailments or from cancer will cease to be legitimate. Since this seems likely to be the case, it is desirable to search seriously into those causes of disability incident to the aging of the body, as exhibited in aging of the heart. Such studies, in whatever ways are possible, now deserve to be expanded.

And how may this be done? If the analysis I have made has value, the situation is this: maladies which result from invasion are on the way to disappearance; congenital defects affect relatively few persons but require further study; they may turn out to be irremediable. The essential remaining cardiac problem centers then upon finding ways of sustaining the performance of the muscle of the heart and in maintaining the health of the blood vessels through which its nourishment is conveyed. It is right in this background to emphasize the fact that far from enough is known now about the physiology of contraction.

and the changes in this which occur with time, and far from enough also in the evolution of the processes that result in destructive lesions of the arteries. On this subject it is desirable accordingly to concentrate research. And if the suggestion is correct, that this

is the direction in which knowledge needs to be expanded, pressure toward this end through scientific investigation ought unremittingly to be maintained. One day the line will be breached and something gained to eliminate the painfulness of slow death.

## OBITUARY

### RECENT DEATHS

**DR. GUSTAVE M. MEYER**, who until his retirement in 1941 was associate in biochemistry at the Rockefeller Institute for Medical Research, New York, with which he had been connected since 1909, died on May 9 at the age of sixty-nine years.

**CHARLES F. JACKSON**, from 1936 to 1942 chief engineer of the mining division of the U. S. Bureau of Mines, died on May 3. He was fifty-nine years old.

**PROFESSOR WILLIAM J. HENDERSON**, of the department

of physics of Purdue University, died on May 10. He was thirty-five years old.

**DR. HERBERT NEWBY MCCOY**, of Los Angeles, from 1917 to 1934 vice-president of the Lindsay Light and Chemical Company, Chicago, previously for sixteen years a member of the faculty of the University of Chicago, died on May 7 at the age of seventy-four years.

**DR. FRED A. HARVEY**, director of research for the Harbison-Walker Refractories Company, known for his work in ceramics, died on April 27. He was sixty-three years old.

## SCIENTIFIC EVENTS

### THE ARGENTINE DECLARATION

IN October, 1943, one hundred and fifty eminent Argentine citizens signed and published a "declaration of effective democracy and American solidarity." The Argentine Government replied by dismissing summarily all signers of the declaration who held official positions. Among the dismissed were Bernardo Houssay, J. T. Lewis and Oscar Orías, heads, respectively, of the institutes of physiology in Buenos Aires, Rosario and Córdoba.<sup>1</sup>

In February, 1945, the Argentine Government decreed the reinstatement of the dismissed professors and officials, and a majority of the one hundred and fifty promptly returned to their posts. Houssay, Lewis, Orías and several others, however, declined reinstatement, pointing out that the new decree not only expressed no regret or explanation of the unjust dismissal, but carried, on the contrary, the implication that the signers had been guilty of a serious offense for which they were now being forgiven. Happily, the situation has been clarified by action of the several universities, Córdoba leading the way. In each case, the university has taken the stand that the dismissal of the professors was an illegal act and an encroachment on the autonomy of the institution. They hold that the professors have never lost their posts. On this ground the dismissed teachers have been invited to resume their duties. Houssay, Lewis and Orías have accepted the invitation, and a regrettable chapter

in the history of Argentine science has thus come to an end.

**ROBERT A. LAMBERT**

### THE ROCKEFELLER FOUNDATION

### REHABILITATION OF THE PHYSICALLY HANDICAPPED

A PROJECT for research on "Social Psychological Rehabilitation of the Physically Handicapped" is the subject of a contract between Stanford University and the Office of Scientific Research and Development recommended by the Committee on Medical Research.

On the research staff of the project are Tamar Dembo, research director; Helen H. Jennings, research associate in psychology; Ralph K. White, assistant director, and Milton Rose, psychiatrist. The Advisory Board, headed by the chairman of the department of psychology, Dr. Ernest R. Hilgard, includes the following members of the department of psychology and of the School of Medicine; Roger G. Barker, Paul R. Farnsworth, George S. Johnson, Donald E. King, Quinn McNamara and Calvin P. Stone.

The project has as its aim the investigation of stigmatizing attitudes toward physical handicaps, through investigation of different degrees of maladjustment as shown in the inter-personal behavior between physically handicapped and non-handicapped people. While emphasis is placed upon the problems of the war-handicapped, the study includes those handicapped in civilian life.

<sup>1</sup> SCIENCE, November 26, 1943, page 467.

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There are also included diverse interview and discussion techniques, group activity experiments, role playing, level of aspiration, value structure and value-analysis methods.

THE AMERICAN CHEMICAL SOCIETY

At a meeting in Washington of the Board of Directors of the American Chemical Society on April 17, it was recommended by the Committee to Consider New Activities of the Society that a proper use of the funds of the society for the advancement of chemistry is the aiding of especially promising individuals in their training as chemists and chemical engineers, the better to enable them as leaders to add distinction to the chemical profession and to ensure our country's welfare. It was pointed out that this program could be fostered through loans, scholarships and fellowships awarded to carefully selected and deserving teaching and student personnel.

To carry out these objectives an educational fund was established, \$500,000 being transferred thereto from the general funds of the society, both corpus and income to be available under proper safeguards to be set up by the Board of Directors. A committee of three directors was appointed to draw up plans for the administration of the fund and to report its findings to the board at its next meeting. Members of the committee appointed are Drs. W. A. Noyes, Jr., C. S. Marvel and Robert E. Swain.

The treasurer was instructed to take the necessary steps to set aside funds for the purpose, and was instructed to pay the necessary expenses of the committee to draw up plans for its administration.

THE AMERICAN ACADEMY OF ARTS  
AND SCIENCES

At the annual meeting of the American Academy of Arts and Sciences, held on May 9 at its house, 28 Newbury Street, Boston, the election of 33 new fellows and five foreign honorary members was announced:

FELLOWS

*Mathematical and Physical Sciences*

Eric Glendinning Ball, associate professor of biological chemistry, Harvard.

Garrett Birkhoff, associate professor of mathematics, Harvard.

Arthur Clay Cope, professor of chemistry, Massachusetts Institute of Technology.

Hardy Cross, professor of civil engineering, Yale.

Robley Dunglison Evans, associate professor of physics, Massachusetts Institute of Technology.

Norman Levinson, associate professor of mathematics, Massachusetts Institute of Technology.

John Lawrence Oncley, assistant professor of physical chemistry, Harvard.

Frederick Emmons Terman, professor of electrical engineering, Stanford.

John Benson Wilbur, professor of structural engineering, Massachusetts Institute of Technology.

*Natural and Physiological Sciences*

Martin Julian Buerger, professor of mineralogy and crystallography, Massachusetts Institute of Technology.

James Morison Faulkner, professor of medicine, Tufts.

Thomas Hale Ham, assistant professor of medicine, Harvard.

Dennis Robert Hoagland, professor of plant nutrition, University of California.

John Robert Loofbourow, professor of biophysics, Massachusetts Institute of Technology.

Herman Augustus Speehr, chairman, division of plant biology, Carnegie Institution.

Henry Crosby Stetson, research fellow in oceanography, Harvard.

John Henry Welsh, Jr., associate professor of zoology, Harvard.

Leland Clifton Wyman, associate professor of physiology, Boston University.

*Social Sciences*

Edwin Sharp Burdell, director, Cooper Union, New York, N. Y.

William Lockhart Clayton, Assistant Secretary of State, Washington, D. C.

Seymour Edwin Harris, associate professor of economics, Harvard.

William Rupert Maelaurin, professor of economics, Massachusetts Institute of Technology.

Henry Allen Moe, secretary general, Guggenheim Foundation.

Talcott Parsons, professor of sociology, Harvard.

Howard Eugene Wilson, associate professor of education, Harvard.

*Humanities*

Samuel Chamberlain, etcher and author.

Edwin Ray Guthrie, professor of psychology, University of Washington, Seattle.

William Alexander Jackson, librarian, Houghton Library, Harvard.

Keyes DeWitt Metcalf, director, Harvard University Library.

George Wiley Sherburn, professor of English, Harvard.

Taylor Starek, professor of German, Harvard.

Charles Lincoln Taylor, Jr., dean, Episcopal Theological School, Cambridge.

Martin Wagner, associate professor of regional planning, Harvard.

*Foreign Honorary Members*

Niels Bohr, professor of theoretical physics, University of Copenhagen.

Sir Harold Spencer Jones, astronomer royal, Greenwich, England.

Alfredo L. Palacios, professor of political economy, University of La Plata.

Dennis Holme Robertson, professor of economics, University of London.

**Tomás Navarro Tomás**, professor of Spanish philology, Columbia.

The following officers were elected for the year 1945-1946:

*President*: Howard Mumford Jones.

*Vice-Presidents*: George R. Harrison, Alfred C. Lane, Ralph E. Flanders, Fred N. Robinson.

*Corresponding Secretary*: Abbott Payson Usher.

*Recording Secretary*: Hudson Hoagland.

*Treasurer*: Horace S. Ford.

*Librarian*: Frederick H. Pratt.

*Editor*: Robert P. Blake.

Dean Joseph Hudnut and Professor Carl J. Friedrich spoke on "The Boston Contest."

## SCIENTIFIC NOTES AND NEWS

**DR. FRANK C. WHITMORE**, since 1929 dean of the School of Chemistry and Physics of the Pennsylvania State College, has been awarded the thirty-fourth Willard Gibbs Medal of the Chicago Section of the American Chemical Society in recognition of his "outstanding contribution as an organic chemist and his vigorous leadership in many organizations devoted to the advancement of chemistry for national benefit." The award is made annually "to any one who, because of his eminent work in, and original contributions to, pure and applied chemistry, is deemed worthy of special recognition."

THE Legion of Merit of the War Department has been conferred on Colonel Cornelius Packard Rhoads, director of the Memorial Hospital for the Treatment of Cancer and Allied Diseases of New York City and for nearly two years chief of the Medical Division of the Chemical Warfare Service. The award is in recognition of the development of methods for combating poison gas and other advances in chemical warfare.

THE Howard Taylor Ricketts prize for "outstanding research on viruses" has been awarded to Dr. Maurice R. Hilleman, of New Brunswick, N. J., in recognition of his work in developing a way of making an anti-serum of value in identifying a recently discovered group of viral agents, carried out in the department of bacteriology and parasitology of the University of Chicago. The award was presented on the thirty-fifth anniversary of the death of Dr. Ricketts, who fell a victim to typhus fever while working on that disease in Mexico. The investigation was supported in part by the Commission on Influenza, the Board for the Investigation and Control of Influenza and other Epidemic Diseases, the United States Army and the John Rockefeller McCormick Memorial Fund of the University of Chicago. Dr. Hilleman is now engaged in research in the field of filterable viruses in the laboratories of E. R. Squibb and Sons.

**DR. IRWIN W. SIZER**, associate professor of physiology at the Massachusetts Institute of Technology, has been awarded a grant of \$5,000 by the Eli Lilly pharmaceutical company for the continuation of his studies on the action of enzymes on the irritant principles of poison ivy and related plants.

It was stated in the issue of SCIENCE for April 16 that the Nobel Prize for physics had been presented on April 11 to Professor I. I. Rabi. The formal presentation by the Minister to the United States of Sweden had been made on December 10, 1944. The presentation of the gold medal, the diploma and the check was made the occasion of a reception at Columbia University on April 11.

**DR. JAMES L. PETERS**, curator of birds of the Museum of Comparative Zoology of Harvard University and assistant secretary of the International Commission on Zoological Nomenclature, has been elected vice-president of the commission in succession to the late Dr. C. W. Stiles, of the Smithsonian Institution, Washington.

THE annual initiation and banquet of the Kappa Chapter of Sigma Xi at Columbia University was held on May 1. Following the reception and dinner, Dr. Harlow Shapley, national president of the society, addressed the chapter on "Infinite Dissipation." Officers elected for 1945-46 were: *President*, Dr. S. R. Detwiler, professor of anatomy, College of Physicians and Surgeons; *Vice-president*, Dr. Walter Rautenstrauch, professor of industrial engineering; *Secretary-Treasurer*, Dr. John S. Karling, professor of botany.

AT Columbia University, Dr. Abraham Wald has been promoted to a professorship of mathematical statistics. P. L. Hsu, of Kunming, China, has been appointed visiting professor of statistics for the semester beginning on January 31, 1946. He will lecture on advanced multivariate analysis and on other fields in mathematical statistics to which he has contributed.

**DR. HARRY MOORE**, director of the research laboratories of Pilkinton Brothers, England, has been appointed to the chair of glass technology at the University of Sheffield to succeed Professor W. E. S. Turner, whose retirement was recently announced.

**DR. WILLIAM W. PETER**, associate professor of public health and chief of sanitary inspection of the department of health of Yale University, has resigned to become director of the training division of the Institute of Inter-American Affairs in Washington.

DR. NORMAN J. VOLK, head of the Department of Agronomy of Purdue University, has become associate director of the Agricultural Experiment Station. He succeeds Dr. W. V. Lambert, who resigned recently to accept a position as assistant administrator of the Agricultural Research Administration of the U. S. Department of Agriculture. Dr. Volk will continue to serve as head of the department of agronomy. Professor Claude Harper, acting head of the department, succeeds Professor Frank G. King, who asked to be relieved of his administrative responsibilities because of ill health. Professor King will continue as a member of the staff.

DR. WILLIAM HENRY HOLLINSHEAD, associate professor of anatomy at the School of Medicine of Duke University, during the summer quarter will be visiting associate of anatomy at the School of Medicine of the University of Tennessee, not at the University of Utah, as incorrectly announced.

DR. F. C. STEWARD, reader in plant physiology in Birkbeck College of the University of London, has a leave of absence and is visiting the United States to take up a temporary appointment as research associate in the University of Chicago. It is stated in *Nature* that the appointment is a sequel to the destruction in an air raid of the research laboratory in plant physiology at Birkbeck College, which had been largely equipped by the Rockefeller Foundation.

DR. G. E. MILLER, organic chemist and technical assistant to the Commanding General, Technical Command, at Edgewood Arsenal, has become actively associated with W. A. Taylor and Company, of Baltimore, of which he was one of the founders.

At the invitation of the Swedish Medical Society, Sir Howard Florey, F.R.S., professor of pathology at the University of Oxford, is lecturing in Sweden on subjects connected with penicillin.

DR. ANTONIO PEÑA CHAVARRÍA, director of the San Juan de Dios Hospital, San José, Costa Rica, is visiting the United States for a period of two months to make a study of medical education. This visit is made under a fellowship from the Association of American Medical Colleges and the John and Mary R. Markle Foundation in recognition of his valuable contribution to the program for giving instructors from medical schools of the United States and Canada practical experience in tropical medicine in Central America.

DR. FRANCIS G. BLAKE, Sterling professor of medicine and dean of the School of Medicine of Yale University, will deliver the Charles V. Chapin Oration. His subject will be "Some Recent Advances in the Control of Infectious Diseases."

THE second William Hamlin Wilder Memorial Lec-

ture of the Institute of Medicine of Chicago will be delivered on May 25 by Dr. Karl Paul Link, professor of biochemistry at the Agricultural Experiment Station of the University of Wisconsin. His subject will be "The Anticoagulant Dieumarol."

DR. DONALD D. VAN SLYKE, chief research chemist at the Hospital of the Rockefeller Institute for Medical Research, New York, gave on May 4 at the Medical College of Virginia, Richmond, the annual lecture of the Brown-Séquard chapter of the Alpha Omega Alpha. He spoke on "The Physiology of the Kidney."

DR. EDMUND VINCENT COWDRY, professor of anatomy at the School of Medicine of Washington University, gave on April 23 the Adam M. Miller Memorial Lecture at the Long Island College of Medicine. His subject was "Microscopic and Chemical Properties of Preeancerous Lesions."

AT the March commencement of the University of Tennessee College of Medicine the address to the graduates was given by Lieutenant Colonel James Barrett Brown, M.C., A.U.S., chief of plastic surgery at the Valley Forge General Hospital, formerly associate professor of surgery at Washington University, St. Louis. The address was entitled "Investment in Personality."

DR. LLOYD L. SMITH, research supervisor of the Division of Game and Fish of the Conservation Commission of Minnesota, spoke at Iowa State College on May 2 on "The Present Status and Trends of Fisheries Biology and Management."

It is reported in *Nature* that the British Secretary of State for the Colonies and the Medical Research Council have jointly created a Colonial Medical Research Committee to advise them on medical research for the benefit of Colonial territories. It is constituted as follows: Sir Edward Mellanby, secretary of the Medical Research Council, *chairman*; Colonel J. S. K. Boyd; Professor P. A. Buxton, professor of entomology, London School of Hygiene and Tropical Medicine; Dr. A. N. Drury, director of the Lister Institute of Preventive Medicine; Brigadier N. Hamilton Fairley; Dr. W. H. Kauntze, chief medical adviser to the Secretary of State for the Colonies; Professor B. G. Maegraith, professor of tropical medicine at the Liverpool School of Tropical Medicine; Dr. B. S. Platt, director of the Human Nutrition Research Unit, Medical Research Council, and Major-General Sir John Taylor. The secretary of the committee is Dr. F. Hawking, of the National Institute for Medical Research, London, N.W.3.

*The Journal of Scientific and Industrial Research* reports that the Government of India has constituted a Scientific Consultative Committee with the following

personnel, under the chairmanship of the Honorable Member for Planning and Development: Sir C. V. Raman, Sir Jnan Ghosh, Professor Megnad Saha, Dr. Nazir Ahmad, Colonel Sir Ramnath Chopra, the Master-General of Ordnance, the vice-chairman of the Imperial Council of Agricultural Research or the Agricultural Commissioner to the Government of India, the Director-General, I.M.S., the director of the Geological Survey and the director of Scientific and Industrial Research. The functions of the committee will be to advise the Government of India on all general questions of policy relating to research which may be specifically referred to it.

THE thirtieth annual meeting of the Optical Society of America will be held at the Hotel Pennsylvania, New York, on October 18, 19 and 20. Should the present Federal restrictions be still in force in October, the meeting would be of local character, and New York City was selected because of the large number of members who reside within the ordinary commuting zone. Attendance from outside the regular commuting zone will be limited to fifty members, in conformity with the definition of a local meeting established by the War Committee on Conventions. In preparation for a meeting of this type, it is proposed to establish a "priority list," giving preference in turn to officers of the society, invited speakers, authors of abstracts submitted for the Cleveland meeting, which was cancelled, authors of abstracts for the October meeting and the membership at large.

THE Pittsburgh section of the Electrochemical Society will sponsor a symposium to be held on May 25 at the Mellon Institute. The subject will be "Polarization and Passivity." The speakers will be Dr. A. Langer, Dr. R. T. Phelps and Dr. E. A. Gulbransen, Westinghouse Research Laboratories; Dr. K. Graham, Graham and Crowley and Association, Inc.; Dr. P. T. Stroup and Dr. R. B. Mears, Aluminum Company of America, and Dr. H. Uhlig, General Electric Company. The meeting will be open to Pittsburgh members of the American Association for the Advancement of Science.

## DISCUSSION

### COMPARATIVE SCIENTIFIC STRENGTH OF UNIVERSITIES

THE recent note by Visher<sup>1</sup> on comparative university strength in scientists starred in "American Men of Science" properly defines its procedures and includes a faint note of caution. It is probable, nevertheless, that many readers will take the data of that note as indicative of the relative scientific faculty

UNDER the joint auspices of the Polytechnic Institute of Brooklyn, the Society of Rheology and the Metropolitan Section of the American Physical Society, a one-day conference will be held at the Polytechnic Institute on June 2 on "The Ultracentrifuge in Highpolymer Research." James Burton Nichols, head of the Section of Physics and research chemist of the Experimental Station of the du Pont Company, will preside at the conference. The speakers will be Professor J. W. Williams, of the department of chemistry of the University of Wisconsin; Professor Charles Beckman, of the department of chemistry of Columbia University, and Dr. Kurt G. Stern, of the Highpolymer Research Bureau of the Polytechnic Institute.

*Nature* states that owing to the generosity of the Rockefeller Foundation of New York, which has for a fifth year in succession provided a grant for the purpose, the Royal Society is in a position to give assistance to scientific societies and associations which, as a result of war conditions, are experiencing financial difficulties in the publication of scientific journals.

SIR WILLIAM HENRY COLLINS, chairman of the Cerebos Salt Company, has made a gift of £100,000 to the Royal College of Surgeons for the endowment of the department of anatomy and for the establishment of a chair of human and comparative anatomy. Last year Sir William gave £100,000 to endow a chair of pathology. The museum and research departments have been damaged during the war. Their maintenance, however, is now assured by the gift, and the college can proceed with its rebuilding plans.

THE International Telephone and Telegraph Corporation has announced the formation of a new organization with an initial capital investment of \$2,000,000 to coordinate more closely its electronic research, including advancements in radio, television and related fields of communication and aerial navigation. The company has been incorporated under the laws of Delaware, with headquarters at Nutley, N. J. E. M. Deloraine, director of the Federal Telephone and Radio Laboratories, has been made president.

strength of the listed institutions. Visher's wording does encourage this interpretation, and this would seem to be the principal reason for making such a tabulation. In fact, such an interpretation is highly unreliable and leads to serious errors in rating of scientific faculties and consequent grave injustice to some of the universities involved.

In the first place, the basic but unstated postulate that starring in "American Men of Science" is a reliable criterion of scientific ability or eminence is

<sup>1</sup> Stephen S. Visher, SCIENCE, 101: 272-273, 1945.

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self open to considerable doubt. It may, however, be granted to be a convenient criterion and probably sufficiently reliable for obtaining an approximate average.

A second point, more important than the first, is that the tabulation includes only scientists first starred in 1933 or later. Obviously a faculty all the members of which were starred before 1933 might now be considerably stronger than one with a high percentage of members first starred in 1944, even though it might have less prospect of enduring eminence. Valid figures for present strength should certainly include all starred scientists now active on the various faculties, regardless of when they were first starred. Even if the intention were to estimate probable future eminence of faculties, the criterion of recent starring would be poor, because age at starring is highly variable and younger men, particularly, often move after being starred.

Most serious of all is the fallacy of taking Visher's column III as an index of "average scientific faculty strength," as Visher seems to invite the reader to do. This column gives the percentage of recently starred scientists in the total faculty. Since only scientists can be starred and since the proportions of scientists (starred and unstarred) on the various faculties are radically different, these figures are completely unreliable as a basis for comparison. For instance, the figure in column III is 1.4 per cent. for Columbia University and 14.3 per cent. for the California Institute of Technology. Without myself attempting a comparison on inadequate data, I venture to claim that the California Institute of Technology has nothing like ten times as strong a scientific faculty as Columbia. At California Institute of Technology most of the faculty consists of scientists eligible for starring. At Columbia only a small proportion of the faculty consists of scientists. The most nearly valid means of comparison would, of course, be based on starred scientists and total scientists, not on starred scientists and total faculty. (Both absolute and relative numbers should, of course, be taken into consideration; a faculty with three scientists, 100 per cent. starred, is obviously not as strong as one with 50, only 10 per cent. of whom are starred.)

The rating by number of alumni starred in or after 1933, given in columns IV-VI of Visher's note, is subject to the same grave objections plus at least two more faults. Here, too, only recently starred scientists are included and the percentages given are based on total numbers of male college students and not, as they should be, either on the numbers majoring in science or the numbers who became professional scientists. An additional pitfall here is that such a figure, even if on a more valid basis, would not measure

present scientific strength of the institution, or strength at any time in the past, but only a rough sort of average for the prolonged period during which scientists destined to be starred in 1933-1944 were being graduated.

Moreover, if these figures for students are to be considered as having any bearing on comparison of the institutions in question, it must be postulated that the institution contributed significantly to the subsequent starring of its students. Such a postulate can be accepted (and then with some reservations) only if the student received his *professional* training at the given institution. Especially in the period in question, most scientists received their professional training in graduate schools. But the figures given are for male undergraduate enrolment in non-professional colleges and for subsequently starred scientists who received their college degrees (evidently their first or bachelors' degrees, not the doctorate) in these institutions. There are one or two other equivocal points, but this, in itself, is enough to brand these figures as completely valueless for any comparison of the scientific strength of the institutions or of their relative success in training scientists.

Neither the data on faculties nor those on students in the note cited should be taken as a basis for comparing the strength or teaching value of the scientific departments of our universities.

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THE AMERICAN MUSEUM OF NATURAL HISTORY

#### THE EFFECT OF MOTION PICTURES ON BODY TEMPERATURE

In the course of an extended study of the variations in the diurnal body temperature cycle, which required ten oral temperature readings per day, it was found that after attending a two- or three-hour commercial motion picture show the subject's temperature was higher than usual for the particular time of the day. Sitting for that length of time under laboratory conditions almost always led to a distinct fall in body temperature, an expected result of muscular relaxation.

To get reliable numerical data, body temperature figures were gathered on two female subjects. The first, a teen-aged girl, attending motion picture shows in the afternoon, every two or three weeks, over a period of over two years, furnished 55 "movie" body temperature readings of 99.00 to 100.15° F, with a mean value of 99.59. Temperatures taken at the same time (about 4 P.M.) on 57 days preceding or following "movie" days, ranged from 97.95 to 99.70, the mean being 98.66° F or 0.93° lower. Another way to treat the temperature figures was to compare the difference between afternoon and basal (getting-up time in the morning) temperatures obtained on

control and on "movie" days. The mean rise in temperature in 54 control days was  $0.73^{\circ}$ , while the corresponding value for 45 "movie" days was  $1.69^{\circ}$ . The differential rise on "movie" days was  $0.96^{\circ}$ , about the same as  $0.93^{\circ}$  obtained by direct comparison, with a *t* value of over 14 (using Fisher's method of statistical evaluation of significance) or one possibility in trillions that the difference was due to chance.

The second subject, a young lady in her early twenties and a "movie addict," attended motion picture shows 29 times in the course of two months, viewing 47 feature films, mostly in the evening, in many cases taking two temperature readings, at 8 P.M. and 10 P.M. Twenty-two 8 P.M. "movie" figures varied from 99.0 to 99.65, with a mean value of 99.42, while 30 corresponding control temperatures fluctuated between 98.40 and 99.40, with a mean of 98.95. The difference,  $0.47^{\circ}$  F., was highly significant (*t* value of 6.24), and the chance of its being gratuitous is one in a billion. Here, too, comparing the differences between the basal and 8 P.M. temperatures in a larger series, the mean rise on 83 control evenings was  $1.15^{\circ}$ , that on "movie" evenings  $1.68^{\circ}$ , a mean differential of  $0.43^{\circ}$  being about the same as by direct comparison (*t* value of 7.28). In this subject the 10 P.M. temperature readings, taken usually at the end of the second feature film, were lower than the 8 P.M. values, the mean of 24 "movie" measurements being 98.91, while 28 control evenings gave a mean level of 98.66, the difference of  $0.25^{\circ}$  being just on the borderline of significance (*t* value of 2.65). It appears that either the body temperature raising effect of the second feature was less than that of the first, or that the normal diurnal fall in body temperature late in the evening was too strong to be completely reversed.

In summary, on the basis of occasional data obtained on many subjects, male and female, and through an analysis of multiple readings on two female subjects, it appears that attending motion picture shows, though looked upon as "relaxation" in the sense of escape from the humdrum reality of existence, is by no means relaxation in the physiological sense. On the contrary, although the spectator remains in a sitting position for two or more hours, the subject-matter of the film evokes an increase rather than a decrease in muscle tension which manifests itself in a highly significant rise in body temperature of one-half to one degree F. It remains to be seen whether the collective change in the body temperature of a preview audience can be used to predict the box-office success of a film.

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## GROWING RUBBER IN COSTA RICA

A PECULIAR paradox of the agricultural economies of Caribbean countries is the high population density and scarcity of agricultural land in the highland areas, while down in the coastal plains there lie tremendous expanses of flat lowlands which for centuries have waited for development. Some people have thought that the populations prefer the highlands because of climate and health factors, but closer inquiry will reveal the main factor to be primarily economics. Tropical lowlands can produce basic foodstuffs like corn, rice and beans, but no one has yet found a permanent export cash crop capable of providing the economic base that is essential for an integrated community growth. Bananas have been tried in spots, but it wears down the soil too fast for permanent communities to really develop. And thus we have gross waste of soil resources in the midst of an acute scarcity.

This problem, which has baffled statesmen for over a century, now promises to be solved, thanks to the efforts of the U. S. Department of Agriculture Rubber Field Station at Turrialba under the leadership of Dr. Theodore Grant. The first thing found was that by a process of cross-breeding it was possible to develop varieties of *Hevea brasiliensis* combining high rubber yield with resistance to fungus attack. Then Dr. Grant convinced a group of scattered small farmers that they could develop rubber plantings of their own by just putting a little spare work over that required to raise their marginal food crops, and letting the station provide the technical knowledge and the planting material at nominal cost. And thus a practically self-sustaining system of rubber cultivation was initiated at very low cost, and without the complications inherent to large corporate organizations, which have never been able to understand, or be understood, by the average Caribbean native.

The small-farm rubber program as developed by Dr. Grant fits nicely into the general scheme of tropical life because it provides a simple system by means of which the average marginal farmer of the lowlands can gradually build himself a definite source of cash income without interfering with his food-raising activities. And the fact that rubber is a permanent crop will encourage the people to stay put in one place and to evolve gradually into integrated communities instead of being mere transient squatters. In other words, rubber bids fair to provide to the tropical lowlands the same type of economic stabilization that the cultivation of coffee has provided to the highlands.

At the present moment there are only seventy-five small rubber farms in Costa Rica, with an average area of around one or two acres each, but the impor-

ent thing is not so much the total acreage as the fact that they are scattered over a wide region suitable for rubber cultivation; and that as such, they provide practical demonstrations and establish the base for the future growth of the rubber industry. It seems to this correspondent that further efforts should be made by the United States Government to encourage and greatly expand this program of grow-

ing rubber on small farms, not only because of the strategic importance of having ample supplies of natural rubber close at hand, but primarily because it provides an inexpensive manner of efficiently developing one of the unused resources of the countries of the Caribbean.

RAFAEL W. KEITH

SAN JOSE, COSTA RICA

## SCIENTIFIC BOOKS

### INDIVIDUALITY

*The Biological Basis of Individuality.* By LEO LOEB. 714 pages. Springfield (Illinois) and Baltimore: C. C. Thomas. Price \$10.50.

THIS is a great and memorable work. The book is a unified presentation of a lifetime of research on certain of the central problems of biology, of an investigation held to with rare tenacity, breadth of view and unity of purpose for nearly fifty years. The beginning was a paper published in 1897 on the transplantation of skin. That paper and its successors opened wide vistas, so that since that date the author, with many different collaborators at different periods, has published more than a hundred papers in technical journals, all touching this field. Now all results are brought together, in this volume, in relation with those of other workers in this field, and in their bearing on general concepts and problems; so that a unified encyclopedic treatise results. The author is conservative and eminently "sound" in his generalizations and conclusions; yet many of them are almost or quite "sensational" in their interest. The book has been under revision in the author's hands for fifteen years. It was first written in 1930 and has been revised or rewritten repeatedly since that time.

When tissues of an individual body are removed and regrafted to the same individual ("auto-transplantation") there is little or no reaction against the transplanted tissue. But if the graft is from another individual, closely related ("syngenesio-transplantation") or of the same species but not closely related ("homoio-transplantation") or is from another species ("hetero-transplantation"), there is a decided reaction of the host against the graft. This is shown mainly by the gathering of lymphocytes and their further activity, and by growth of connective tissue and blood vessels into the graft. The special character of this reaction and its intensity varies with the relationship of the graft and host individuals, the reaction being slight if the relationship is close, greater as the relationship is more distant. Thence emerges the central concept of the work, the "individuality differential" or in more general terms the "organismal differential."

The difference between graft and host—their individuality differential—is obviously dependent on the different genes which they possess; it is greater as the number of differing genes is greater. Investigations in genetics have been largely devoted to the effects of genes taken separately. In the individuality differential Loeb finds a single unified effect of a large number of genes acting together. The character of the individuality differential is affected—so the evidence indicates—by many genes; perhaps by all those present in the individual. Thus two individuals differing in any number of genes show individual differentials of a corresponding degree of difference.

The individuality differential is "common to all the various tissues and organs of an individual," though its manifestation may differ in intensity in different tissues. Similarly, there are also characteristics that are common to all members of a species, genus, order or class; "these may be called species—genus—order—class differentials," all being in their totality designated as "organismal differentials." Such group differentials present a means of determining or judging the relative degree of relationship of organisms. Seemingly of a different character are "organ and tissue differentials," distinguishing different parts of the same individual. All these categories are justified and elucidated by extensive illustrative experimental results described in the body of the book.

In a twenty-three-page introduction is presented a valuable systematic outline or summary of the concepts and conclusions to which the work leads, together with a generalized account of the experimentation on which they are based. A first chapter of nine pages deals more technically with the aims and methods of the investigations: how the reactions of host and graft are manifested, methods most useful in the analysis of the organismal differentials; what experimental animals are most satisfactory, and methods of evaluating the different reaction grades. Later chapters are devoted to detailed description and discussion of experiments and results which justify the concepts and conclusions reached.

The author is led to deal extensively with reactions that are induced by the impact of parts of one in-

dividual on another, yet differ from those in which the individual differentials play the chief role. He has chapters or sections on serological reactions, on immunity reactions, on blood groups, on cancer, on fertilization, on hormones, on hybridization and on other topics. Most or all of these receive illumination from experimental results presented, or from comparisons. The work thus becomes a veritable encyclopedia of the main factors and processes in development.

The book furnishes material that will be of interest to geneticists as well as to students of ontogenetic and phylogenetic development; in particular to spe-

cial students of immunity, of inbreeding, of regeneration, of ageing, of cancer, of animal toxins, of tissue culture, of blood groups, of adaptations, of the relationships of groups of organisms to other groups.

The last part, on "Psychical-social Individuality," presents in three chapters the general and philosophical views of the author on what the significance of it all is for the world of man. Chapter headings are "The Physiological Basis of the Psychical-social Individuality"; "Individuality and the World," and "The Evolution of Individuality." There is an extensive bibliography and a good index.

H. S. JENNINGS

## REPORTS

### WAR RESEARCH AT MELLON INSTITUTE, 1944-5

THE investigational personnel, experience and facilities of Mellon Institute have been utilized fully in wartime essential research programs during its fiscal year ended February 28, 1945, as brought out in the thirty-second annual report of the director, E. R. Weidlein. Some of the vital projects and accomplishments in the pure research department and on industrial fellowships of the institute will be referred to in this summary, which supplements previous wartime records.<sup>1</sup> All the activities of the organization are non-profit.

#### RESEARCH IN PURE CHEMISTRY

The work of the institute's department of research in pure chemistry has been largely devoted to chemotherapeutic studies, with particular emphasis on the synthesis of new drugs of possible antimalarial activity, for professional, military and public benefit.

*Synthesis of New Antimalarial Drugs.* The novel hydroxyethylating agents developed for use with apocupreine have been applied to a variety of new compounds, some of which are possibly useful as therapeutic agents. Substituted lepidyl-pyridinium and quinolinium bromides and lepidyl mercaptans have been made for testing as antimalarials. Basically substituted diphenyl ethanolamines and substituted mandelic thioamides have also been prepared as antimalarials.

Of the two synthetic antimalarials that have achieved clinical usage, namely, quinacrine and pamaquine, the latter is representative of the most active chemotherapeutic agents so far discovered for the treatment of malaria. But the adoption of pamaquine to any extent in actual medical practice is precluded, since last year the U. S. Army advised against its routine use because the margin of safety between

<sup>1</sup> SCIENCE, 97: 445-7; 99: 389-91, 409-11.

therapeutic and toxic doses is too small. This experience has led to the departmental search for modified compounds which will retain high antimalarial activity but will be much less toxic to the host. The possibility of obtaining a much less toxic drug of this type is an additional attraction in that pamaquine has been found to have true prophylactic action at the toxic-dose level.

This research on the detoxification of pamaquine has been patterned after the work previously done in this department in detoxifying the antipneumococcal agent "Optochin," work which resulted in the discovery of hydroxyethylapocupreine. A comprehensive plan has in fact been undertaken to synthesize and study hydroxyethyl analogs of the pamaquine series. Several compounds in this class have been made and one substance has considerable promise.

Sulfur derivatives of quinoline, including some thioethers, have been prepared. The selection of the compounds investigated was influenced by the possibility that, where toxicity is low, certain representative derivatives might advantageously be submitted for testing in relation to other fields of tropical medicine. Certain substituted 2-styrylquinolinium quaternary salts are known to have pronounced chemotherapeutic properties, but the corresponding bases have not been studied. Consequently ten new bases of this type have been synthesized.

Four new 4-(*p*-dialkylaminostyryl)-quinolines have been prepared. As it has been the experience here that the introduction of a hydroxyethyl group into the molecule greatly diminishes toxicity, 6-hydroxyethylapocupreine has been synthesized and some of its derivatives are being prepared. The corresponding 6-hydroxy derivatives have also been made. Likewise in progress is a study of the preparation of various lepidyl and quinaldyl carbinols and their derivatives in order to learn the effect of a carbinol bridge in compounds of this type. A somewhat similar carbinol

bridge is, of course, present in quinine. As certain quinoline azomethines possess some structural resemblances to quinine, quinacline and pamaquine, and because the quaternary salts of some show both bactericidal and trypanocidal action, an investigation in this field has been undertaken.

**Hydroxyethylmorphine.** With the assistance of the new alkylating agents mentioned, the hydroxyethyl ether derivative of morphine has been prepared and some of its pharmacological properties have been determined. Introduction of the hydroxyethyl group was again shown to cause a marked lowering of systemic toxicity. In mice, hydroxyethylmorphine was  $\frac{1}{5}$  as toxic and  $\frac{1}{5}$  as convulsant as morphine,  $\frac{1}{11}$  as toxic and  $\frac{1}{17}$  as convulsant as the methyl ether of morphine (codeine), and  $\frac{1}{20}$  as toxic and  $\frac{1}{22}$  as convulsant as the ethyl ether (dionine). The analgesic power of hydroxyethylmorphine in mice, subjected to a pain stimulus induced by heat, was substantially equivalent to that of codeine and dionine. Derivatives of morphine are known that are 5 to 10 times as analgesic as and 10 to 20 times more toxic than the parent alkaloid. When these materials become available, they will be subjected to the hydroxyethylation procedure.

**Drug Standardization.** The 13th revision of the "Pharmacopoeia of the United States" is now under way. Of the 93 new admissions 21 have been assigned to the subcommittee on organic chemicals, which is conducting pertinent investigations in the institute. Because war conditions in the Pacific have detached our normal source of natural l-menthol, the physical and chemical properties of synthetic racemic menthol have been studied. A method has been developed for the determination of iodine in organic compounds and a procedure for determining iodine in thyroid has received favorable industrial comment. There is a steady increase in parenteral medication, calling for a vast supply of ampuled solutions or of dry compounds in ampules for the preparation of injections, such as penicillin and the organic arsenicals. It is imperative that containers made of highly insoluble glass shall be used for such purposes, and accordingly the ASTM and the USP have speeded up their cooperative study on the chemical methods of analysis. Mellon Institute is one of the six organizations participating in this investigation.

#### INVESTIGATIONS IN APPLIED SCIENCE

**New Physical Methods and Devices.** Research has demonstrated the potential speed of a process for separating gas mixtures by diffusion into a fast-streaming vapor. A procedure has been evolved for determining hydrogen in gases with a thermal conductivity apparatus. The spectrometric analysis of gases has had much attention. The physical and

thermodynamical properties of sulfur vapor are being tracked down, commencing in a study of density. Methods proposed for measuring surface areas of porous adsorbents have been studied critically. A procedure has been worked out for determining thermal conductivities at low temperatures. An automatic torque machine has been developed to record rapidly and accurately frictional resistance to rotary motion. Engineering benefit has come from the completion of a program on frictional losses in vaned elbows of asbestos ducts that has resulted in these losses being reduced to an absolute minimum.

**Useful Ceramic Progress.** Research has been devoted to the treatment of dry air-set mortars so as to prolong the period during which they may be stored, and this investigation has led to a product with decidedly improved keeping properties. By comparison, the new mortar may be stored approximately four times as long as the present-day material. Through searching study efficiency has been imparted to the manufacture of "Garerete," "Garspar" and "Gartex," with improvements in the quality of these products. The applications of "Garspar" in ceramics have been increased, especially in the making of china and sanitary wares; the uses of "Gartex" have been extended in rubber and plastics technology. A new process has been devised for the manufacture of "Garsand," a promising glass batch ingredient. Under contract with the Office of Production Research and Development of the War Production Board, there have been developed wire-wound resistors qualified for employment by the Armed Services.

**Solving War Problems in Metallurgy.** An investigation has been begun on the reactions occurring during the sintering of iron powder compacts. Refinements have been made in metallographic procedures for examining such compacts and also iron powder particles. Research on compacts has eventuated in the installation of an industrial physical testing laboratory, and certain of their properties, e.g., tensile strength, have been correlated with the variables occurring in the manufacturing processes. Manganese powder (99.9 per cent.) and also steel powders have been developed from work in the institute. The properties and uses of copper powders are being investigated minutely.

"Ferrocando," a research creation, minimizes segregation and breaks up inclusions in cast iron and also serves as an effectual deoxidizer in steel. The corrosion of metals by sulfur is a recently started inquiry. Pickling inhibitors are under comprehensive investigation. A galvanizing flux has been invented that retards materially the formation of dross during the hot-dipping process. A combination limestone-lime process, which can provide substantial savings in many localities, has been developed for treating waste

pickle liquor. A process yielding chemically pure gypsum, a hydrated iron oxide suitable for sintering, and a relatively pure magnesia from waste pickle liquor and dolomitic lime has been completed on a laboratory scale. Current investigation indicates that magnetic iron oxide of pigment quality can be produced from waste pickle liquor by a simple procedure with low operating costs.

Harnessed tightly to war are research and development on special type mortar shells, rockets and pressure vessels. Captured enemy pressure vessels have been investigated in cooperation with the War Metallurgy Committee and the Armed Forces. A program on the production of chromium has been resumed after an intermission caused by emergency work. New alloying possibilities of magnesium with other metals and particularly the improvement of the cast and wrought properties of magnesium alloys are getting fundamental attention. The precision casting of metal alloys for numerous critical applications has benefited from studies of the use of ethyl silicate in sand molding. Research on electrode coating practice has moved on. Packaging tests have been conducted on a wide variety of products in substitutes for tin collapsible tubes, such as aluminum, tin-coated lead and lead. Internal protective coatings for tubes have also been studied. Improved methods are now at hand for the application of internal coatings of waxes in collapsible tubes. Investigational work on closures has resulted in a satisfactory adhesive for cementing liners into canteen caps.

*Contributions to Coal Chemistry.* A practical investigation is under way on aspects of the combustion of anthracite that are of consequence in domestic heating. Research is quite active on problems concerning bituminous coal derivatives, including the recovery of compounds from coke-oven gas, the elimination of wastes, the improvement of quality of products and the industrial uses of these chemicals. A study of the impurities in "nitration benzene," the most important commercial grade, has been completed, revealing that the principal contaminants are naphthenes. A speedy and accurate method has been composed for determining hydrocyanic acid and certain of its derivatives in gaseous, liquid or solid state. A project pertains to the recovery of thiocyanates from solutions. A new process for making guanidine nitrate has been announced.

Research on the rheological properties of various tar products has been continued. An outcome of utility has been the introduction of a pitch compound of modified flow characteristics, suitable for the protection of metal products, such as corrugated roofing and siding, flat and V-crimp sheets, and associated constructional accessories. The desulfurization of naphthalene is in the pilot-plant stage. A method

has been contrived for determining small amounts of sulfur in naphthalene. Studies have been begun on the oxidation of ethylnaphthalene. A new procedure has been found for making vinylnaphthalene, which has promise in plastics technology. Cyclopentadiene, one of the recently investigated coal chemicals, is now recovered by a number of coke plants for use in the production of synthetic resins. A novel approach has been found to the separation of the constituents of anthracene cake. Improvements have been made in the preparation of vinylcarbazole. Progress has been accomplished in the synthesis of picolines and vinyl derivatives of pyridine and in research on the oxidation of lutidines and picolines.

*Pathfinding in Petroleum Projects.* A new type of still has been designed that gives very striking effects in fractionation; the separation is much better than any so far obtained under vacuum. Research has been conducted on the betterment of methods for separating individual paraffin hydrocarbons of higher molecular weight. The physical properties of waxes are being investigated fundamentally. A mathematical study has been completed on the influence of high rates of shear on the viscosity of lubricating oils. Good progress has been made on the characterization of crude oils as related to their geological environment. An investigation on the physical chemistry of olefin reactions has been advanced. Research has defined the synthesis and properties of 1,1,3-trimethylcyclopentane, a new hydrocarbon. Some fifty alkylated phenols have been identified by finding the properties and x-ray diffraction spectra of their phenylisocyanate derivatives.

The synthesis of liquid hydrocarbons from gases is being investigated by another group. Physical methods have been elaborated for the instantaneous analysis of gaseous mixtures of as many as five components. The extraction of hydrocarbons has been studied with unusual solvents manifesting high degrees of selectivity. The reaction of sulfur with solvent extracts from petroleum stocks has been found to lead to an asphalt-like solid of promise in filling joints and in caulking. The program on nickel compounds and catalysts has been expanded, especially with reference to their applications in the petroleum industry. Research and development have been carried forward on filters, electric refrigeration units and vacuum stills used in controlling the proper condition of machine tool coolants. Equipment has been devised for the collection by froth flotation of grinding waste dispersed in soluble oil emulsions. Studies have been completed on aircraft crankcase oil filters and on appliances for handling and conserving carbon-removing and washing solutions in aircraft engine-repair depots.

*Novel Synthetic Lubricants.* Through collaboration

with the Bureau of Aeronautics, Navy Department, there have been evolved new and improved instrument lubricants of real value. Processes have been devised and demonstrated for making one of these novel lubricants on a manufacturing scale. There has been gained a background of information and experience that points to the development of still better aircraft instrument lubricants as the program proceeds.

At the start of this research it was ascertained that synthetic organic chemicals were the most promising sources for such new lubricants with strict properties. Accordingly several hundred compounds were synthesized and studied extensively, and from the most promising of them 185 blends were prepared. The best compositions determined by laboratory examination were then tested under operating conditions by Naval Air Stations and instrument manufacturers. It was next decided to transfer the procedure for making one of these oils from the laboratory to a unit plant and to introduce such alterations in the processing as became necessary. From this work has come a very satisfactory method that yields a high quality product.

Another program has enabled the production of chemicals for the improvement of hydraulic fluids and low-temperature lubricants of value to the Armed Forces. Experience earned in this research has been followed in the revision of specifications for Army Ordnance hydraulic fluids. The cooperative testing of extreme pressure additives has been carried out for a government agency to provide superior products.

*A Harvest of Food Developments.* Research has been concluded on the proteolytic enzyme activity in chicken eggs. An economic industrial process for drying yeast is at the production stage. Studies on improving the quality of dry active yeast have been going forward constantly. Another investigation is on the value of yeast as a source of antibiotic agents. New synthetic vitamin-D agents are receiving research. Investigational work is in progress on conditions influencing molds and infections in bread. A new dried cereal for infant feeding is in production. A novel pre-cooked baby cereal has been investigated clinically and found satisfactory. In another study strained green soybeans have evinced good nutritive value and other favorable characteristics for inclusion in infant foods. Advancement has been made in research on carbohydrate preparations for modifying milk for infant feeding.

Observations indicate that the phospholipids from cottonseed resemble soybean lipositol more closely than they do other phospholipids previously reported as plant constituents. Soybean protein hydrolyzates have been investigated as flavoring agents for prepared food products. Work is being pursued on processing soybean flakes for the production of pro-

teins especially suited for various industrial applications. Novel granular adsorbents for sugar refining have entered pilot-plant development.

*Research-Woven Textile Events.* The buoyancy and other distinctive qualities of fibrous materials have been studied for military purposes. Fundamental advances have been made in a program on cotton properties. Sizes for the knitting of hosiery have been investigated very near to mill operations. Resin coatings for fibers have been under research from all standpoints. Pleasing results have been attained in increasing permanently the strength of thread by plastics, without imparting stiffness, and in making molded spools. New treatments of woolen felts against heat, water, certain chemicals and abrasion have supplied materials of usefulness. Research on the felting properties of fur and on the standardization of relevant tests and grades has been quite beneficial. Accomplishments have been effected in improving pearl-button machinery and in attacking chemical problems in pearl-button technology. Studies are being conducted on factors influencing detergent action and on the synthesis of detergents with special properties indicated thereby.

For the benefit of the domestic front, commodity standards specialists of the institute have worked with the government in helping to conserve and to standardize home-essential materials. Advisory service has been rendered to the Research and Development Branch, Office of the Quartermaster General. Large experience in the appraisal of consumer goods has made this aid useful in the correlation of laboratory data and field and service test results on new products developed for the Quartermaster. Cooperation has also been extended to the Office of Civilian Requirements, War Production Board, in its program for supplying more adequate quantity and quality in "cost-of-living" textile products.

*Advances in Wood Products and Paper.* Research on lignin has been concerned with the preparation of utilizable derivatives. Wood glues are getting expansive investigation; the gluing of treated (such as creosoted) woods is likewise under study. Sawdust moldings are being investigated in a far-reaching project. Waxes, new resins and intrinsically grease-resistant materials in eleven groups have been employed experimentally for integrally greaseproofing carton and boxboard stocks. Progress has indicated that such stocks are definite possibilities within permissible cost limits. The improvement of GR-S rubber for use in paper saturation has moved forward, particularly as to heat resistance and non-staining. The three primary grades of such paper are being applied as leather replacements and in shoe-material and garment manufacturing. The technology of a new direct line paper is being defined in a pilot plant.

*Investigational Acquisitions for Plastics Technology.* A miniature plant for making bentonite plastics has been constructed as an adjunct to the laboratory work. Service tests have demonstrated the utility of new coriaceous plastics in several essential industries. Preformed plastic, developed in a 5-year program, is produced from a mixture of 99 per cent. water and 1 per cent. wood fibers and a phenolic resin, beaten together and then strained by vacuum through a screen to preform to the desired shape, as an airplane wing tip. The wet preform is next oven-dried and molded under heat and pressure. An investigation has been completed on the reaction of sulfur with olefins. Research is continuing on other organic plastics containing sulfur. Allyl alcohol has been studied as an intermediate in synthetic resin production.

Much work has to do with processing and utilizing plastics. Precision casting, molding-laminating techniques and drying are being investigated. Fibrous reinforcing fillers for molding mixtures are receiving study. Other projects relate to new plasticizers. Plastics for lock-nut manufacture have been examined from all aspects. The relative temperature stability of stressed plastics is a concluded research. Another program pertains to the improvement of plastic piston rings and to the development of bearings and bushings fabricated of synthetic resins. The properties of various types of electrical tapes constitute a new investigation, and research is being continued on the aging characteristics of industrial tapes. Synthetic waterproof adhesives are being studied for specific purposes.

A research has covered the characterization and utilization of byproduct oils resulting from butadiene manufacture from alcohol. The infrared analysis of butadiene has been dealt with comprehensively. New uses are being sought for styrene. Amines are under trial in compounding synthetic rubber. Surface-treated pigments prepared by the "Micerizer" process are proving of interest as fillers in synthetic rubber and as carriers for insecticides.

*Better Protective Coatings.* An investigation of "Vinylite" resin solution coatings has been accelerated to cope with critical problems arising from allocation trends. Suspensions of these resins in organic media have been developed and adapted to the manufacture of battery separators, to metal foil, wire, paper and cloth coatings, and to the molding of soft rubberlike plastics of many kinds. Improvements have been made in vinyl resin coatings for "Nylon" and in the use of plastic film in packaging.

Protective coatings secured by research are now being widely employed, in army and naval services, to line concrete aviation gasoline storage tanks and airplane wing tanks. New synthetic resins and resin

combinations have been formulated into protective coatings with special properties for steel shell casings, gun barrels, airplane propellers, bomb shackles, food containers and other war materials. More economical methods of coating formulation have been investigated. Evaluative tests have been started on synthetic resin coatings for use in hot-water tanks and pipe lines. Fundamental studies have been continued on marine coatings, with particular attention to the prevention of fouling by marine organisms.

*Research on Organosilicon Derivatives.* A fellowship was founded by the Macbeth-Evans Glass Company in 1931 for the development of certain types of glass composition. Upon the merger of this donor with the Corning Glass Works the problem of coating glass blocks with a cement-adherent material, assigned to the fellowship, was successfully solved. The fellowship was then asked to carry on cooperative research with the Corning laboratories on the synthesis of organosilicon compounds intended as impregnants for electrical glass tape. This investigation brought useful findings. A series of organosilicon oxide fluids was synthesized that proved to be the basis for other diversified preparations. Resinous compounds of utility in impregnating and molding were also discovered. As this collaborative research went forward it was realized that efficient production would require the assistance of experience in technicochemical procedure. The Dow Chemical Company undertook to evolve production methods and the outcome was the formation of the Dow Corning Corporation, which is manufacturing these materials in a large new plant at Midland, Mich.

The products resulting from this teamwork vary widely in physical characteristics. Fluids are being made that have high heat stability and low freezing points, with exceedingly small slope to the temperature-viscosity curve. Greases have been developed that have found uses as lubricants or electrical sealing compounds where corrosive and high-temperature conditions prevail. Water-repellent compounds are available for application to ceramic insulators and the like. Resins are in production that have given rise to a new class of electrical insulation, unique for its heat-resistance and moisture-proofness. The laminating type of resin employed in conjunction with glass cloth affords sturdy panels that are electrically non-tracking and are not flammable. Relaxation of secrecy orders permits the statement that temperature-resistant elastic types of silicones have been under development here for several years and that some of them are now on the market. Practically all the materials produced were originally completely allocated to war purposes and have helped in the solution of problems presented by the Armed Forces.

*Fellowship Research for Public Health.* The petro-

latum gauze announced a year ago is now implanted in production. Intermediates for sulfa drugs and antimalarials have been synthesized and put at the disposal of medicinal research organizations. Pentanediene is available to the pharmaceutical industry. Special amines have been made in a pilot plant for use in the synthesis of a new anesthetic. A novel process for preparing ethyl-phenyl malonic ester has been worked out. The synthesis of intermediates for theophylline production has been improved and the synthesis of papaverine is undergoing research along new lines.

The range-finding test is offered as a discerning solution to the problem of probing the toxic hazards of new chemical compounds before their uses justify large expenditures upon detailed studies. Coal-tar derivatives of promise as disinfectants have been appraised and ways of using them are under study. A new insecticide mentioned last year is in small-scale production. The synthesis of insect repellents has been supplemented and progress has been accomplished in the search for satisfactory means of utilizing existing repellents by combat forces. The repelling property of "Hubbellite" for specific insects is another project.

*What Is Being Done in the Maintenance of Man-power.* Industrial Hygiene Foundation, which has its headquarters at Mellon Institute, has added to the

forward health movement through its numerous services and activities for the maintenance of manpower among its member companies and the industrial fields in general. Most important have been plant hygiene investigations to appraise working conditions for their possible effects upon health, and to provide preventive engineering measures to control noxious and obnoxious exposures in workplaces. Sixty of these surveys were conducted during the year, mainly in the East and Middle West, and the projects ranged from several days to over a month in duration.

Numerous studies have been made of soldering operations. Several chemical dermatitis problems have been overcome through the coordination of field investigations with experimental studies by ten dermatologists. In other research electron photomicrographs of air-borne asbestos dust have disclosed that the particles are preponderantly fibrous and that the ultimate fiber is about 0.01 micron in diameter. In addition to its plant hygiene surveys and research, the foundation, with the collaboration of the U. S. Public Health Service, has carried on a program, started in 1940, to help reduce sick absences in the industries. Systematic course of action in industrial hygiene demands concrete knowledge not only of the amount of sick absenteeism, but also of when, where and why it occurs.

W. A. HAMOR

## SPECIAL ARTICLES

### CRYSTALLIZATION OF SOUTHERN BEAN MOSAIC VIRUS

SINCE the first chemical isolation of tobacco mosaic virus in 1935,<sup>1</sup> a fairly large number of plant<sup>2,3</sup> and animal<sup>4,5,6</sup> viruses and certain bacteriophages<sup>7</sup> have been obtained in more or less pure form. In spite, however, of widespread success of the purification procedures, only three viruses, tobacco mosaic,<sup>1</sup> tomato bushy stunt<sup>8</sup> and tobacco necrosis<sup>9</sup> viruses, have been

<sup>1</sup> W. M. Stanley, SCIENCE, 81: 644, 1935; *Phytopath.*, 26: 305, 1936.

<sup>2</sup> W. M. Stanley and R. W. G. Wyckoff, SCIENCE, 85: 181, 1937; W. M. Stanley, *Jour. Biol. Chem.*, 129: 405, 1939.

<sup>3</sup> H. S. Loring and R. W. G. Wyckoff, *Jour. Biol. Chem.*, 21: 225, 1937; F. C. Bawden and N. W. Pirie, *Brit. Jour. Exp. Path.*, 19: 66, 1938; H. S. Loring, *Jour. Biol. Chem.*, 26: 455, 1938.

<sup>4</sup> J. W. Beard and R. W. G. Wyckoff, SCIENCE, 85: 201, 1937.

<sup>5</sup> J. W. Beard, H. Finkelstein and R. W. G. Wyckoff, SCIENCE, 86: 331, 1937.

<sup>6</sup> R. W. G. Wyckoff, *Proc. Soc. Exp. Biol. and Med.*, 36: 71, 1937.

<sup>7</sup> H. Bechold and M. Schlesinger, *Biochem. Zeitschr.*, 36: 388, 1931; J. H. Northrop, *Jour. Gen. Physiol.*, 21: 35, 1938.

<sup>8</sup> F. C. Bawden and N. W. Pirie, *Nature*, 141: 513, 1938; *Brit. Jour. Exp. Path.*, 19: 251, 1938.

crystallized. Considerable interest is therefore attached to the isolation of a fourth virus, southern bean mosaic virus, in crystalline form. This virus, which was first described and studied by Zaumeyer and Harter,<sup>10</sup> is sufficiently stable that it may be purified and concentrated by the methods commonly employed for the purification of proteins. Perhaps it is of significance that some of the crystalline forms, the shape of the particles and the thermostability of southern bean mosaic, tomato bushy stunt and tobacco necrosis viruses are similar. On the other hand, their host ranges and cross protection tests indicate that they are not closely related.

Purified preparations of southern bean mosaic virus were obtained by fractionating the juice from infected Bountiful bean plants. The fractionation was carried out either by alternating cycles of high- and low-speed centrifugation or by chemical treatment. The chemi-

<sup>9</sup> N. W. Pirie, K. M. Smith, E. T. C. Spooner and W. D. McClement, *Parasitology*, 30: 543, 1938; F. C. Bawden and N. W. Pirie, *Brit. Jour. Exp. Path.*, 23: 314, 1942.

<sup>10</sup> W. J. Zaumeyer and L. L. Harter, *Phytopath.*, 32: 438, 1942; *Jour. Agr. Res.*, 67: 305, 1943.

cal fractionation consisted of concentration by precipitation with  $(\text{NH}_4)_2\text{SO}_4$  and then resolution in water, removal of certain impurities by treatment with 30 per cent. alcohol in which the virus remained soluble, and then removal of the virus by a second precipitation with  $(\text{NH}_4)_2\text{SO}_4$ . Further purification was sometimes accomplished by precipitation with  $\text{MgSO}_4$ .

Crystallization was carried out in the following manner. Highly purified preparations containing about 15 or 20 mg/cc of the virus were brought to about 20 per cent. saturation with respect to  $(\text{NH}_4)_2\text{SO}_4$  or  $\text{MgSO}_4$  by addition of the solid salt and centrifuged for three hours in a Bauer and Pickels type<sup>11</sup> high-speed centrifuge at 24,000 r.p.m. The supernatant, which contained practically no virus activity, was poured off and discarded. To the clear, glassy pellets in the bottom of the centrifuge tubes was added one or two drops of distilled water and the tubes were then held overnight at about  $3^\circ \text{C}$ . As the pellets absorbed water they slowly became opaque and on examination were found to contain masses of crystals. The crystals were of one of two types, the type obtained depending upon conditions not yet fully known. Careful examination under the microscope suggests that both types belong in the orthorhombic system, yet this conclusion is only tentative since accurate measurements of the interfacial angles have not been made. They may be referred to as a rhombic prism (Fig. 1) and as a rhombic bipyramid combined with two pinacoids (Fig. 2).

The suspension containing the crystals was removed and more water was added, two drops at a time, until all the virus in the tubes was removed. In this way there was obtained a mass of crystalline material, which settled out on standing. The mother liquor was pipetted off. The crystalline fraction, which still contained a small amount of mother liquor, was suspended in 0.5 saturated  $\text{MgSO}_4$  or  $(\text{NH}_4)_2\text{SO}_4$ . On addition of the salt solution, the small amount of virus that had remained in solution precipitated as an amorphous fraction. On dilution with an equal volume of water the amorphous material rapidly dissolved and the crystals were then removed by slow-speed centrifugation. Several washings in this manner served to remove all traces of the amorphous material. The washings were done rapidly in order to prevent the crystals from dissolving, since they are readily soluble in water or dilute salt solutions.

Crystals that were washed free of non-crystallized virus and dissolved in  $\text{H}_2\text{O}$  to the extent of about 1 mg/cc gave a positive biuret and xanthoproteic test and a negative test with Molisch's and Fehling's solu-

<sup>11</sup> J. H. Bauer and E. G. Pickels, *Jour. Exp. Med.*, 64: 503, 1936.

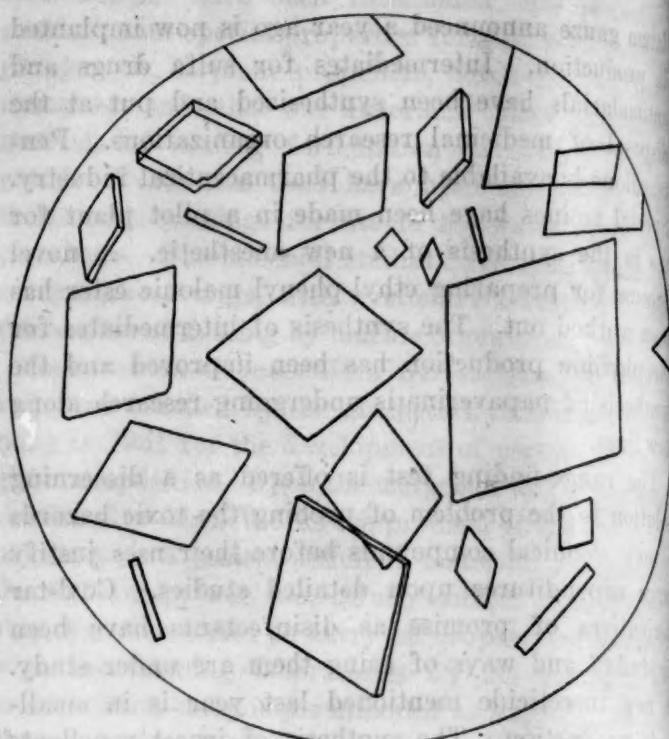


Fig. 1.

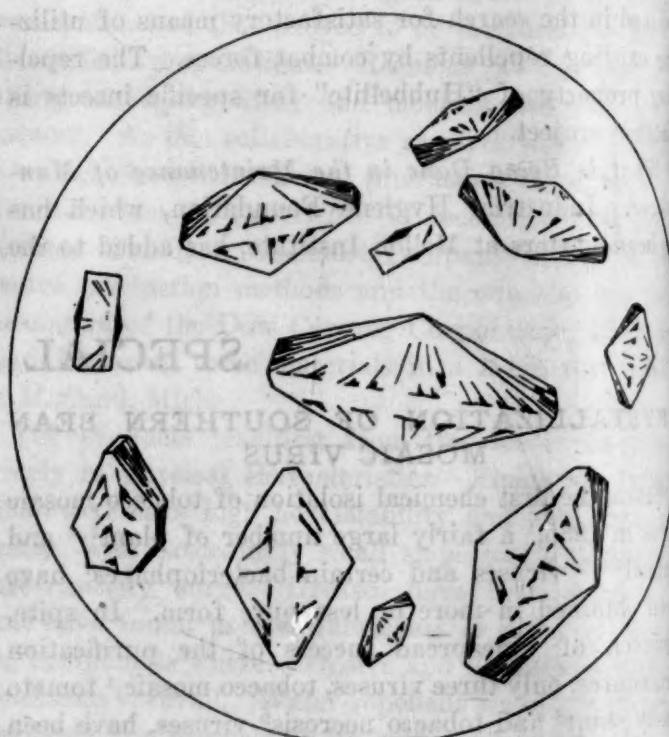


Fig. 2.

Figs. 1 and 2. Diagrammatic representation of crystals of southern bean mosaic virus. Fig. 1 shows the rhombic prisms magnified about 500 times. Fig. 2 represents the rhombic bipyramids at a magnification of approximately 750. Solutions of both types of crystals were infectious at a concentration of about  $10^{-8} \text{ gm./cc}$ .

tions. With Millon's reagent such solutions formed a precipitate that failed to turn red on heating. The glyoxylic reaction was negative in dilute solutions, but concentrated solutions of the virus gave a positive reaction very much weaker than that of egg albumin.

Solutions of the crystalline material produced characteristic symptoms of southern bean mosaic when used to inoculate Bountiful beans. On Early Golden

Cluster beans they produced lesions at concentrations as low as  $10^{-8}$  gm/ce. Table 1 shows the results of

TABLE I

ACTIVITY OF THE BIPYRAMIDAL CRYSTALS (A), THEIR MOTHER LIQUOR (B), THE RHOMBIC PRISMS (C) AND THEIR MOTHER LIQUOR (D) AT CONCENTRATIONS BETWEEN  $10^{-4}$  AND  $10^{-8}$  GMS./CC AS INDICATED BY THE NUMBER OF LESIONS PRODUCED ON 24 LEAVES OF EARLY GOLDEN CLUSTER BEANS

Log. Concentration	Lesions			
	A	B	C	D
-4	4060	2584	3350	2565
-5	1362	810	1098	694
-6	148	231	238	67
-7	33	31	14	6
-8	27	10	11	2

one test of the comparative infectivities of the rhombic prisms and bipyramidal crystals and the mother liquors from each of these. In the preparations used for the test much of the virus had remained in the mother liquors, only from 10 to 30 per cent. of the total having been obtained as crystals. The data show no significant differences between the activities of the crystals and their mother liquors. All four preparations were highly active.

Purified virus preparations appeared to be essentially homogeneous when studied in a high-speed centrifuge, an electrophoresis apparatus and a diffusion apparatus.<sup>12</sup> Concentrated solutions did not show stream double refraction when allowed to flow under crossed polaroid plates. This indicates that the virus particles are not elongated rods or plates, a conclusion which is borne out by calculation of the shape of the particles from sedimentation and diffusion data. In the presence of  $MgSO_4$  or  $(NH_4)_2SO_4$ , the virus is considerably more soluble at low than at high temperatures. Virus completely precipitated as an amorphous fraction with a minimum amount of salt at room temperature goes into solution in about an hour at  $3^\circ C$ . In this respect it is similar to tomato bushy stunt<sup>8</sup> and tobacco necrosis<sup>9</sup> viruses.

The chemical tests that have been made indicate that the crystalline material is mostly protein. The homogeneity of the material indicates it to be relatively free from impurities. That the material is not a normal constituent of bean plants is shown by the failure on several occasions to isolate any such material by subjecting the juice of healthy bean plants to the treatments described above. The fact that thoroughly washed crystals are infectious when diluted to  $10^{-8}$  gm/cc indicates that they represent the virus itself and not some by-product of virus activity.

The results therefore show that southern bean mosaic virus consists of essentially spherical particles small enough and uniform enough to crystallize under appropriate conditions. The fact that the virus has been crystallized is not considered sufficient evidence

<sup>12</sup> Data to be published.

on which to decide whether it is animate or inanimate in nature.

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## **INACTIVATION OF THE IRRITANT TOXICANTS OF POISON IVY AND RELATED COMPOUNDS BY TYROSINASE**

WORK of the past years, chiefly by Majima,<sup>1</sup> Hill et al.,<sup>2</sup> and Mason and Schwartz,<sup>3</sup> has resulted in the isolation, identification and synthesis of certain of the skin irritants of poison ivy, poison oak and related plants of the *Anacardiaceae*. These compounds have been shown to be phenols or catechols characterized by a long unsaturated side chain attached to the ring (see Fig. 1). Since the toxic properties of the molecule are due in part to the presence of OH groups

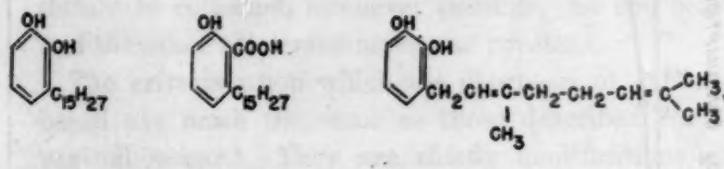


Fig. 1

in the ring,<sup>4</sup> one of the better methods of treatment of skin poison ivy involves oxidation of such groups with strong oxidants such as ferric chloride and potassium permanganate. It seemed possible, however, that the same results might be obtained using innocuous agents such as enzymes. Since the phenol oxidases are not highly specific<sup>5</sup> (attacking such different compounds as mono- and polyphenols, tyrosine and even certain of the sex hormones<sup>6</sup>), it seemed possible that this type of enzyme might also oxidize phenolic groups of the toxic poison ivy irritant as well as related compounds.

In this study were used a large number of partially purified and concentrated commercial poison ivy extracts as well as pure compounds of structure and toxic properties known to be related to the active principle (urushiol) of poison ivy. The enzyme solutions employed were very active and highly purified mushroom tyrosinase.<sup>7</sup> The reaction was studied by measuring oxygen consumption in the Barcroft res-

<sup>1</sup> R. Majima, *Ber.*, 55 B: 172, 1922.

<sup>2</sup> G. A. Hill, V. Mattacotti and W. D. Graham, *Jour. Am. Chem. Soc.*, 56: 2736, 1934.

<sup>1</sup> H. S. Mason and L. Schwartz, *Jour. Am. Chem. Soc.*, 64: 3058, 1942.

<sup>4</sup> (a) I. Toyama, *Jour. Cut. Dis.*, 36: 157, 1918. (b) H. Keil, D. Wasserman and C. R. Dawson, *Jour. Exp. Med.*, 80: 275, 1944.

<sup>5</sup> J. M. Nelson and C. R. Dawson, *Adv. in Enz.*, 4: 99, 1944.

<sup>6</sup> S. Ansbacher, "Vitamins and Hormones," 2: 215, 1944.

<sup>7</sup> We are greatly indebted to Dr. J. F. Nelson of Columbia University for the tyrosinase preparations.

pirometer at 37° C. It was necessary to have the toxic principle in both the experimental and control cups, since a very slow auto-oxidation of the various toxicants could be demonstrated even in the absence of the enzyme. The results of a typical experiment are shown in Fig. 2, from which it appears that on

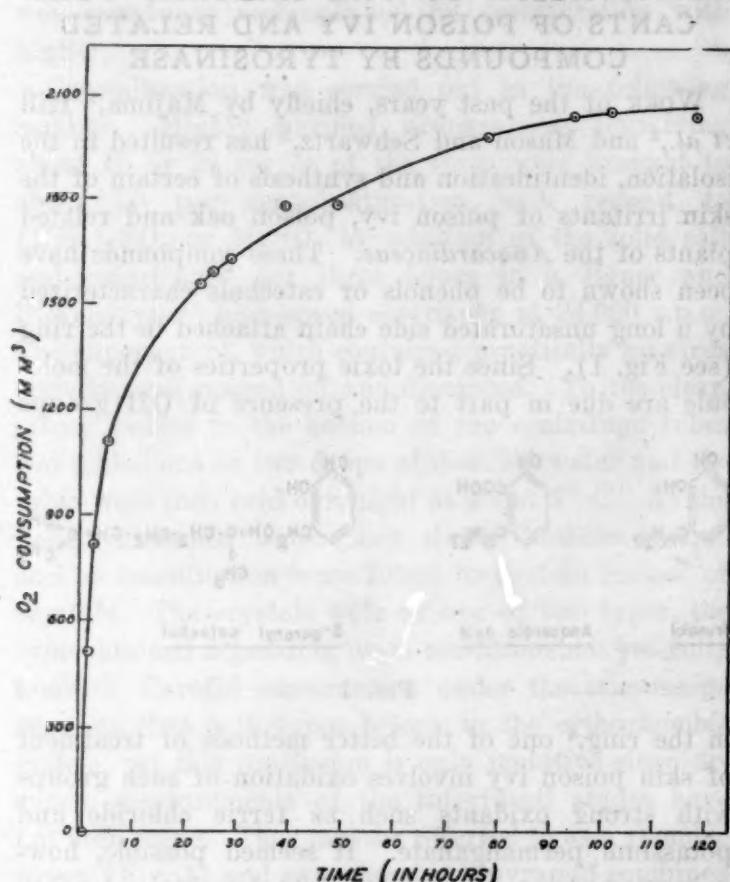


FIG. 2. The effect of tyrosinase on oxygen consumption by partially purified and concentrated poison ivy extract (Lederle) is shown. The experimental flask of the Barcroft respirometer contained 1 ml poison ivy extract, 0.1 ml tyrosinase and 3.2 ml buffer, pH 7.3. The control flask contained 1 ml poison ivy extract plus 3.3 ml buffer.

the addition of the enzyme the consumption of oxygen proceeds very rapidly at first and then more slowly after a few hours. Comparable results have been obtained with all the different poison ivy preparations as well as with all the pure toxic compounds, using three different tyrosinase extracts.

Confirmatory evidence that the various toxic molecules have undergone catalytic oxidation by tyrosinase is furnished by the fact that during the reaction the solution gradually darkens in color. This increased pigmentation is probably due to the enzymatic oxidation of the phenolic groups to quinones, since it can be shown that during the reaction there is a marked decrease in the amount of phenolic groups present as measured with the FeCl<sub>3</sub> test.<sup>8</sup>

Experiments on human and guinea-pig skin were performed to see whether or not the tyrosinase had

<sup>8</sup> R. D. Coghill and J. M. Sturtevant, "An Introduction to the Preparation and Identification of Organic Compounds," McGraw-Hill 1st. edition 1936, page 144.

effected any change in the dermatitis-producing properties of poison ivy and related skin irritants. The guinea pigs were plucked and sensitized<sup>9</sup> before use, and for both humans and guinea pigs the patch test<sup>10</sup> was utilized. This involved the application of a small amount of the digest (usually dissolved in ether) onto a small area of the forearm or leg (humans) or flank (guinea pigs). An identical application to an adjacent area was made with untreated material or one containing inactivated enzyme. Comparisons of the two areas for the next seventy-two hours were made for erythema, vesicle formation, pruritis and spreading. When amounts of irritant just sufficient to produce mild symptoms were used, it was possible in the majority of cases to demonstrate a clear difference between the two areas. The control area coated with toxicant showed much more severe dermatitis than the experimental area which was covered with toxicant inactivated by enzyme. In several studies there was no apparent dermatitis at all in the experimental area. Results with guinea pigs were similar to those with humans.

The problem of the inactivation of poison ivy toxicant on the human skin was studied in four experiments by applying simultaneously to the skin for 4 hours the poison ivy concentrate plus tyrosinase in buffer solution. The control area was the same except that boiled enzyme was used. The area treated with active enzyme showed much less dermatitis than the control, indicating partial inactivation of the toxicant on the skin by tyrosinase. If successful results can be obtained in the future by applying the enzyme some time after the toxicant has reacted with the skin (even after erythema has been produced) then a new method of treating poison ivy dermatitis will be available. A detailed report of the present study will be published elsewhere.

**Summary:** The action of mushroom tyrosinase on the oxidation of the irritant principles of poison ivy and on related toxic compounds has been demonstrated by measuring oxygen consumption, color change, decrease in phenolic groups and reduction in dermatitis-producing properties of these compounds on human and guinea-pig skin. The action of tyrosinase on poison ivy toxicants occurs both *in vitro* and on the human skin.

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<sup>9</sup> (a) F. A. Simon, *Jour. Immun.*, 30: 275, 1936. (b) J. L. Jacobs and M. L. Weicker, *Proc. Soc. Exp. Biol. and Med.*, 38: 726, 1938. (c) E. K. Stratton, *Calif. and West. Med.*, 54: 115, 1941.

<sup>10</sup> E. L. Keeney, S. Sunday, L. N. Gay and K. Lynch, *Bull. Johns Hopkins Hospital*, 69: 482, 1941.

## URINE SEDIMENT SMEARS AS A DIAGNOSTIC PROCEDURE IN CANCERS OF THE URINARY TRACT<sup>1</sup>

THE demonstration that cancer of the uterus undergoes constant exfoliation which renders possible its recognition in a vaginal<sup>2, 3, 4</sup> or endometrial<sup>5</sup> smear led us to investigate the possibility of using a similar method for the diagnosis of malignant tumors of other organs.

The urinary tract appeared to be most suitable for such an investigation. One would expect that in a cancerous lesion of one of the urinary organs superficial cancer cells would become exfoliated into the excretory ducts and be carried out by the urine.

The fact that cells from a cancer of the bladder have been seen in smears prepared from the vaginal fluid<sup>6</sup> proves that cancers of the urinary organs undergo superficial desquamation. Recently, we have been able to ascertain that such cells may also be found in smears prepared from fluid aspirated from the female urethra.<sup>7</sup> For this we employed a technique similar to the one used for preparing endometrial smears.<sup>5</sup> A fine metal cannula<sup>8</sup> was introduced in the urethra and the fluid was aspirated with a lock syringe. The fluid was spread on a slide and then fixed and stained in the same way as a vaginal or endometrial smear.<sup>4, 5, 9</sup>

This method permits the demonstration of cancer cells in lesions of the female bladder and urethra. Its use is, however, limited, as it can not be applied to other organs or in men. For this reason we began to explore the possibility of developing a satisfactory technique for demonstrating cancer cells in the sediment of centrifuged urine.

The results were very gratifying and soon our technique was crystallized as follows: Approximately 40 cc of urine were collected in a tube and mixed immediately with 10 to 20 cc of 95 per cent. alcohol. This secured a good fixation and preservation of the cellular elements. The urine was centrifuged for ten minutes at twenty thousand revolutions per minute.

<sup>1</sup> This work was supported by the Commonwealth Fund of New York.

<sup>2</sup> G. N. Papanicolaou, *Proc. Third Race Betterment Conference*, p. 528, 1928.

<sup>3</sup> G. N. Papanicolaou and H. F. Traut, *Am. Jour. Obstet. and Gynec.*, 42: 2, 193-206, 1941.

<sup>4</sup> G. N. Papanicolaou and H. F. Traut, The Commonwealth Fund, New York, May, 1943.

<sup>5</sup> G. N. Papanicolaou and A. A. Marchetti, *Am. Jour. Obstet. and Gynec.*, 46: 3, 421-2, 1943.

<sup>6</sup> Papanicolaou's unpublished data.

<sup>7</sup> The first urethral smears were prepared with the co-operation of Dr. Allister M. McLellan and Dr. J. Scott Gardner of the Department of Surgery (Urology) of Cornell Medical College and the New York Hospital.

<sup>8</sup> W. H. Cary, *Am. Jour. Obstet. and Gynec.*, 46: 3, 422-4, 1943.

<sup>9</sup> G. N. Papanicolaou, *SCIENCE*, 95: 2469, 438-9, 1942.

It is preferable to do the centrifuging without waiting too long, although a specimen may be kept for several hours, and even days, without deteriorating too much.

After centrifugation, the supernatant fluid is removed (preferably by aspiration) and the sediment is spread with a wire loop on glass slides which have been thinly filmed with albumen. The fixation of the smears is important and must be done before complete drying, in a solution of equal parts of 95 per cent. alcohol and ether. There, the slides may be kept for any length of time, although a fixation of five to ten minutes is sufficient. The staining procedure is similar to that used for vaginal smears.<sup>9</sup>

Catheterized urine specimens are generally preferable to voided specimens. When cancer of the kidney or ureter is suspected, it would be desirable to obtain some urine through cystoscopic catheterization of the ureter. In prostatic lesions two specimens of urine should be collected, whenever possible, the one before and the other after massaging the prostate.

The criteria upon which the diagnosis of cancer is based are much the same as those described for the vaginal smear.<sup>4</sup> They are chiefly modifications and abnormalities of the nucleus (enlargement, anisonucleosis, fragmentation, hyperchromatosis, granular arrangement of the chromatin, prominence of nucleoli, etc.), changes affecting the cytoplasm (basophilia, vacuolation, leucocytic infiltration, etc.), and significant deviation of cells from their normal size and form.

Thus far eighty-three cases have been investigated.<sup>10</sup> Of these, seventy were men and thirteen women. The results will be reported in detail in a subsequent paper. They offer conclusive evidence that in neoplasms of the bladder, prostate, kidneys and of other organs of the urinary tract, the superficial desquamation is of such a proportion as to permit a diagnosis by urine sediment smears. The type and location of the tumor are not always clear. A longer and more detailed study is necessary for the final classification of the various types of cancer cells which are encountered.

Of the eighty-three cases, twenty-seven have been reported as positive for neoplasm on the basis of smears without any knowledge of clinical findings. In twenty-four of these (88.88 per cent.) the smear diagnosis was confirmed by biopsy (21 cases) or clinically (3 cases). In the remaining three (11.12 per cent.) the final diagnosis remained obscure. There was no case in which the smear was reported as conclusive for malignancy which definitely did not have a neoplasm.

<sup>10</sup> Most of the specimens were obtained through the courtesy of Dr. A. R. Stevens and Dr. A. L. Dean, of the Urological Departments of the New York and Memorial Hospitals.

In the group of cases where the smear was inconclusive or negative, the percentage of correct diagnosis was lower (about 60 per cent.). This might be interpreted as indicating that in some tumors the exfoliation is less pronounced, as has already been observed in tumors of the uterus.<sup>4</sup> When the number of exfoliated cells is small, their presence may more easily escape attention. In most instances the smear diagnosis was based on the examination of a single voided specimen of urine. It is likely that a greater accuracy would be obtained if the tests were repeated and more catheterized specimens were used.

The small number of cases examined thus far does not permit a thorough evaluation of this diagnostic method. However, we consider the results as very encouraging. It is particularly gratifying that twenty-one (88.88 per cent.) of the twenty-seven cases reported as positive were also positive from a clinical standpoint and that false positives were absent.

The cytology of the urine smear presents its own characteristics and these will require a thorough and systematic study. We intend to carry this work further and hope that at some future time we will be able to include our findings in a monograph, comparable to the one published on vaginal smears.<sup>4</sup> In the meantime, we feel that other investigators should have the opportunity of applying this new technique and of exploring its possibilities. This prompted us to give an account of our observations in this short preliminary report.

The great simplicity of this method, the ease of obtaining material without inconveniencing the patient and its inexpensiveness are great assets to its wider experimental or clinical application. It might prove particularly useful whenever repeated examinations are needed, either for clarifying an obscure diagnosis or following up the results of operations or treatments, as in hormonal therapy of prostatic carcinomas.<sup>11</sup> After further evaluation, it might seem advisable to include this test in periodic examinations such as those conducted in public health clinics for the purpose of detecting early or unsuspected neoplasms.

Despite the technical simplicity, the urine smear method of diagnosis, like the vaginal and endometrial smear methods, is rather difficult when it comes to the interpretation of the findings, and special training is

<sup>11</sup> It should be noted that estrogenic treatment causes a significant change in the cellular makeup of the urine sediment, corresponding to that caused in the vaginal secretion (G. N. Papanicolaou and E. Shorr, *Am. Jour. Obstet. and Gynec.*, 31: 5, 806-34, 1936). This consists in the appearance of cells showing marked acidophilia, pyknosis of the nucleus, cytoplasmic granules and increased glycogen content. The cancer cells, when present, stand out and make a striking contrast to the normal cells. Similar findings in the vaginal smear of cervical carcinomas following estrogenic therapy have been reported previously<sup>4</sup>.

required. At its present stage, it should not be considered as a final method of diagnosis. Clinical application must await further evaluation, and treatment should not be based entirely on the results of this test. A corroboration by biopsy, whenever possible, is strongly advised.

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#### NOTE ON THE ADSORPTION OF THROMBIN ON FIBRIN

EARLY studies on the action of thrombin and fibrinogen showed that there is a quantitative relationship between the concentration of thrombin and the amount of fibrin formed.<sup>1,2</sup> The data caused many to doubt Alexander Schmidt's view, which held that thrombin is an enzyme, because it was argued that if thrombin combines with fibrinogen to form fibrin, it is not an enzyme. Later the idea developed that such observations could have been explained on the basis of adsorption, and recently Wilson<sup>3</sup> has found that 5.1 units of thrombin disappear from solution with each mg of clotted fibrinogen. He regards this as an adsorption phenomenon.

Actually he studied only a very limited range of the variables, presumably because an adequate amount of thrombin was not available. We have extended the work and have found the relationship shown on Fig. 1.

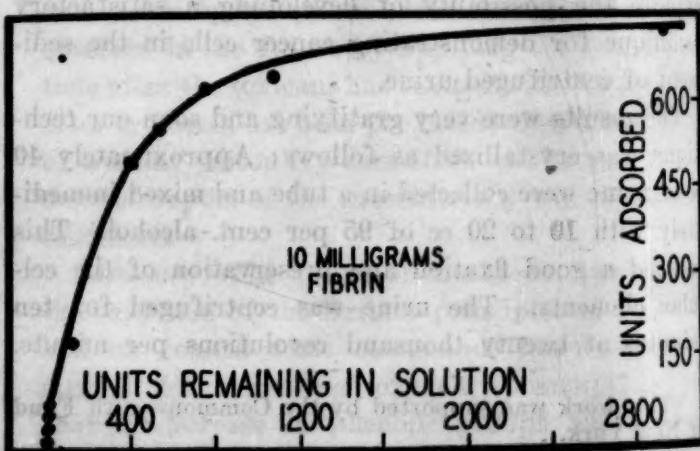


FIG. 1. The adsorption of thrombin on 10 mg fibrin, at room temperature, with a solution volume of 2 cc.

When thrombin clots fibrinogen large amounts of the former are removed from solution, and the quantity removed depends upon the original concentration of the thrombin solution. The curve showing the equilibrium relationships has the appearance of an adsorption isotherm. The new data thus support the view that thrombin is removed from solution by ad-

<sup>1</sup> W. H. Howell, *Am. Jour. Physiol.*, 26: 453, 1910.

<sup>2</sup> L. A. Rettger, *Am. Jour. Physiol.*, 24: 406, 1909.

<sup>3</sup> S. J. Wilson, *Arch. Int. Med.*, 69: 647, 1942.

sorption. An impressive feature of the results is the surprisingly large amount of thrombin which can be removed from solution. For instance, 10 mg of fibrin removed 750 units from a solution originally containing 3,750 units. We may assume 1,400 units per mg dry weight for the specific activity of thrombin<sup>4</sup> and calculate in terms of weight that 10 mg of fibrin removed about 0.53 mg of thrombin.

The results were obtained by using thrombin prepared from bovine plasma as described by Seegers,<sup>5</sup> and fibrinogen prepared by cold alcohol precipitation. The protein in the fibrinogen solution was 98 per cent. clottable with thrombin. The thrombin and fibrinogen

preparations were found by test to be free of anti-thrombin. A solution of fibrinogen in 0.9 per cent. NaCl was adjusted to contain 10 mg fibrinogen per cc. One cc of this solution was added to 1 cc of thrombin solution (various concentrations) in such a way as to produce virtually instantaneous mixing. After 10 minutes the fibrin was removed with a glass rod and the remaining thrombin was measured quantitatively.<sup>6</sup>

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## SCIENTIFIC APPARATUS AND LABORATORY METHODS

### AN EASILY ASSEMBLED MACHINE FOR MAKING COTTON PLUGS FOR CULTURE TUBES

A NUMBER of years ago Dr. H. W. Batcheler, of the Wooster Experiment Station, Wooster, Ohio, demonstrated to the Ohio Academy of Science a machine for the rolling of cotton plugs for culture tubes. Apparently this has not been published, and the writer has not seen the apparatus. As manpower shortages and cotton shortages have developed, the need for such a machine has become increasingly evident. As a result of this, a machine has been developed which is so efficient it is thought others might be interested.

The essential unit of our machine is a Waco Power Stirrer<sup>1</sup> which has two shafts, one running at 300 r.p.m., the other at 600 r.p.m. The faster of the two is the more satisfactory. The only additional requirement is a foot-controlled rheostat for starting, stopping and controlling the speed of the motor. We use an old foot control from an electric sewing machine. This is wired in series with the motor and provides positive control. The actual spindle on which plugs are rolled is a three and one-fourth inch applicator stick which has enough one-inch gummed paper tape rolled on one end to make it fit the quarter-inch chuck available with the stirrer motor. As the applicator stick gradually wears smooth it is necessary to roughen it slightly from time to time with the edge of a sharp knife blade.

We use University Plugging Cotton from the Rock River Cotton Company, Janesville, Wisconsin. This is spread out and strips, as wide as the length of the plug to be made, are cut lengthwise of the roll. This method of cutting assures the fibers running length-

wise of the strip. For test-tube plugs it is desirable to decrease the thickness of the strip by separating it into two layers of approximately equal thickness to assure ease in manipulation. The end of such a strip is brought in contact with the rotating applicator stick and a little pressure starts the roll. The motor is run slowly until the plug has accumulated sufficient cotton. The cotton strip is then pulled loose from the plug and the plug is tightened by applying very light pressure with the thumb and three first fingers held parallel to the rotating plug. A test-tube is then pushed on the rotating plug and the exposed end of the plug is shaped with the thumb and finger to make the fibers compact so the plug will not be pulled apart in use. The motor is then stopped and the plug is removed from the applicator stick while still in the test-tube by pulling both away from the motor.

With a little practice it is possible to make about 150 plugs per hour. The plugs are of any desired firmness and can be used time after time, thus effecting a great saving in cotton. The labor cost per plug is very low and considering the long service which such a plug will give, the final cost is less than for conventional methods of plugging.

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### MICROVISCOMETER

USUAL methods for viscosity determination require specimens of considerable volume. In dealing with small samples, e.g., biological fluids, the simple device described permits rapid, accurate determinations on volumes of less than 0.1 ml.

Measurements are made in terms of resistance to the torque developed by a small synchronous, self-starting

<sup>4</sup> W. H. Seegers and D. A. McGinty, *Jour. Biol. Chem.*, 146: 511, 1942.

<sup>5</sup> W. H. Seegers, *Jour. Biol. Chem.*, 136: 103, 1940.

<sup>1</sup> Wilkins-Anderson Company, 111 North Canal Street, Chicago, Illinois.

<sup>6</sup> W. H. Seegers and H. P. Smith, *Am. Jour. Physiol.*, 137: 348, 1942.

electric clock motor. Under a uniform AC potential (110 volts, 60 cycle current) the motor develops a definite amount of power which is sufficient to maintain its own phase relationship with the AC current, plus an additional force, sufficient to overcome the torque resistance of a viscous fluid. When electrical resistance is introduced, however, a point is reached where the current is insufficient to maintain a synchronous relationship.

The motor is mounted in such a position that its rotor turns in a horizontal plane. A cylindrical platform (1 to 2 cm in diameter) is made from lucite or other plastic rod, and is mounted in concentric fashion on the rotor. A similar stationary member is held by bracket above the rotating platform and is provided with a screw mechanism to vary the clearance between the two members. A variable radio-type resistor

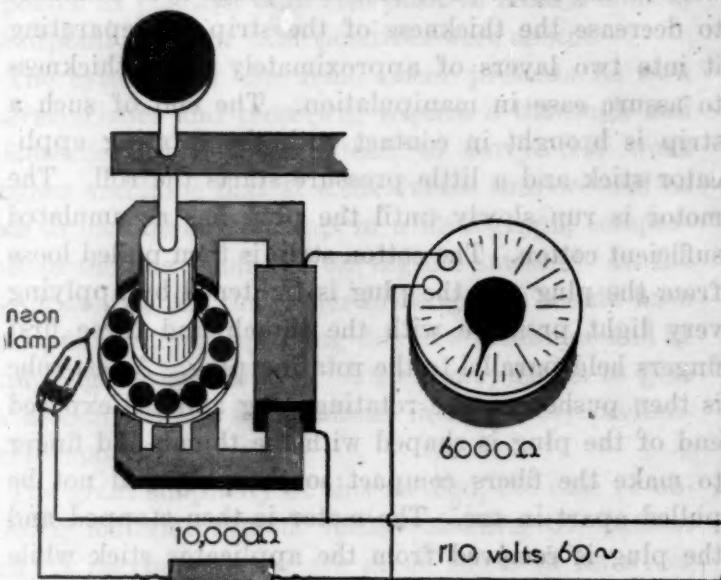


FIG. 1

(preferably wire-wound) is connected in series with the motor, and a small neon lamp is provided, to scan stroboscopically the speed of the rotor.

In making a determination, clearance is first adjusted to a suitable value ( $\pm 1$  mm) using a gauge metal "feeler." The specimen is then introduced between the opposed surfaces by pipette and the motor is started with no resistance in the circuit. Resistance is then cut in slowly while observing the stroboscopic pattern of the rotor. In the light of the neon lamp it will appear stationary; as the end point is reached this rotor pattern suddenly breaks. The resistor dial setting is then correlated with data derived from determinations upon fluids of known viscosity.

Refinements of this apparatus include a constant voltage source, demountable rotor platforms in various diameters with annular troughs to collect any overflow, stroboscopic disc for scanning in lieu of the rotor itself, resistor dial calibrated in centipoises.

The chief possible source of error lies in torque changes due to heating of the resistor after prolonged

operation. This may be overcome by intermittent use or by use of a precision type variable resistor.  
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#### THE USE OF DOUBLE-CYCLE A AND B SCALES ON STRAIGHT SLIDE RULES<sup>1</sup>

THE index of the single-cycle, movable C scale on straight slide rules is shifted (or replaced by the other index) essentially to extend the length of the single-cycle, fixed D scale, as the figures of the product or quotient sought are outside the single logarithmic cycle (but always in an adjoining one). This shifting may be eliminated, without loss in accuracy, on rules having folded C and D scales (or CF and DF scales) by using these scales essentially to extend the length of the D scale from 1 to 1.314 cycles. On other straight rules the shifting may be eliminated, with reduction in accuracy to half (but still with sufficient accuracy for most purposes), by the use of the double-cycle A and B scales present on practically all slide rules. The use of the folded scales is described in most slide-rule manuals, but the use of the double-cycle A and B scales for multiplication and division is not, or at least it is not stressed, probably because the procedure is only half as accurate as the use of the single-cycle scales and because of the similarity of the procedures to those on the single-cycle C and D scales.

The possibility of so using the A and B scales must be known to most slide-rule users, but realization of the lower accuracy of this procedure or oversight probably accounts for the rare use of these double-cycle scales for multiplication and division. The reduction in accuracy from their use, for many purposes, is far outweighed by the convenience of not having to decide which index to use and not having to shift indices in multiplying or dividing by the same factor. In multiplying or dividing by the same factor on the A and B scales, after setting the B scale, it is merely necessary to move the indicator, an operation that can be done by one hand on rules which have an indicator that rides along the top of the rule.

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<sup>1</sup> Published by permission of the Director, Bureau of Mines, U. S. Department of the Interior.

#### BOOKS RECEIVED

CARTER, GEORGE F. *Plant Geography and Culture History in the American Southwest*. Illustrated. Pp. 140. Viking Fund, Inc., New York. 1945.

MOORE, ARTHUR R. *The Individual in Simpler Forms*. Illustrated. Pp. x + 143. University of Oregon Press. \$1.25. 1945.

WERTHEIM, E. *Textbook of Organic Chemistry*. Second edition. Illustrated. Pp. xiv + 867. The Blakiston Company. 1945.